University of Alberta

The Role of Computed Tomographic Angiography in Subarachnoid Hemorrhage, And in the Assessment of Carotid Stenosis

by

Glenn B. Anderson

A thesis submitted to the Faculty of Graduate Studies and Research in partial fulfillment of the requirements for the degree of Master of Science

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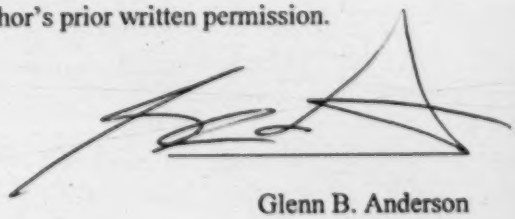

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Abstract

Introduction: A new investigative modality, computed tomographic angiography (CTA), is compared to the current standard digital subtraction angiography (DSA) for the detection of intracranial aneurysms and cerebral vasospasm following subarachnoid hemorrhage (SAH) and for the detection of carotid artery bifurcation disease.

Methods: Patients suffering SAH underwent CTA and DSA. The CTA and DSA exams were compared for the detection and characterization of cerebral aneurysms and cerebral vasospasm. Patients suffering cerebrovascular accidents underwent Doppler ultrasound, CTA, and DSA of the carotid bifurcation. These exams were compared for the detection and characterization of carotid stenosis.

Results: CTA was found to be highly sensitive (90%) and specific (100%) for aneurysm detection. CTA was able to replace DSA in 48% of patients suffering SAH. CTA was highly sensitive (95%) and specific (95%) for detecting none or severe vasospasm in proximal arterial locations. CTA was highly sensitive and specific (>90%) for detecting >50% carotid stenosis or 100% stenosis, but was less so for detecting 50-69% or 70-99% stenosis.

Conclusions: CTA is highly accurate in detecting cerebral aneurysms in the setting of SAH and at least half of patients require only CTA. CTA was accurate in detecting none or severe vasospasm in proximal arterial locations. CTA was excellent for detecting >50% or 100% carotid stenosis.

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Introduction

A) Intracranial Aneurysms and Subarachnoid Hemorrhage

The dictionary definition of aneurysm is " a localized dilatation of the wall of a blood vessel" (21). Aneurysms occur at a variety of sites throughout the human body, but to neurosurgeons intracranial arterial aneurysms are of particular interest. Intracranial aneurysm morphology can be saccular, fusiform, or dissecting. Saccular aneurysms are of prime concern to the neurosurgeon as these may be surgically obliterated. The etiology of intracranial arterial saccular aneurysms is multiple. Hemodynamic factors (pulsatile flow at branch points, high flow, increased pressure) causing degeneration of the arterial wall, are thought to be the most common etiology for most saccular aneurysms (94). Other etiologies of aneurysm formation include structural factors (media and elastica defects in the artery wall), genetic factors (familial aneurysms, genetic syndromes with abnormal blood vessel walls), traumatic causes (penetrating and nonpenetrating injuries), infectious causes, neoplastic causes, and radiation induced causes.

Intracranial aneurysms occur in typical locations. Approximately 90% of intracranial aneurysms occur in the anterior circulation (ie. internal carotid artery circulation). The other 10% occurring in the vertebrobasilar system (78). Aneurysms in the anterior circulation most commonly occur at three sites: the anterior communicating artery complex, the middle cerebral artery bifurcation, and the origin of the posterior communicating artery. Aneurysms in the vertebrobasilar system most commonly occur at the basilar artery tip and at the origin of the posterior inferior cerebellar artery.

Both ruptured and unruptured cerebral aneurysms can produce symptoms. The overall incidence of cerebral aneurysms ranges from 1% to 5% in autopsy studies (32, 4, 62). The incidence of aneurysm rupture is approximately 10 per 100,000 population (31). Rupture of an aneurysm spills blood into the subarachnoid spaces of the brain (fig. 1-3). Patients may present with a wide spectrum of symptoms ranging from headache to coma to death. Approximately 15% of patients with a ruptured aneurysm die before making it to hospital (94). Of those patients who survive to receive medical intervention, 50% will rebleed within 6 months (95). Given the natural history of a ruptured aneurysm the

treatment of choice is surgical obliteration by placing a metallic clip across the aneurysm neck, thus eliminating blood flow into the aneurysm.

In patients with a ruptured cerebral aneurysm the direct effect of the primary hemorrhage is the major source of morbidity and mortality (35). Other major causes of morbidity and mortality include rebleeding before surgical intervention, and cerebral vasospasm. Mayberg (52) defines vasospasm as "the insidious onset of delayed focal or diffuse narrowing of large capacitance arteries at the base of the brain following hemorrhage into the subarachnoid space". Vasospasm has a typical time course, with onset between 3-5 days after the hemorrhage, maximal narrowing at 5-14 days, and gradual resolution over 2-4 weeks (93). Angiographic vasospasm has been reported to occur in approximately 50% of subarachnoid hemorrhage patients (1) with 20-30% being symptomatic (36). Of the symptomatic patients, roughly 50% will sustain a permanent cerebral infarction secondary to narrowing of the arteries. Vasospasm needs to be reliably and promptly diagnosed in order to prevent permanent neurological deficits.

At present, the standard of care for investigation of cerebral aneurysms and vasospasm is digital subtraction angiography (DSA). However a new modality, computed tomographic angiography (CTA), has become available and is being applied to these areas. CTA will be the focus of this review.

B) Carotid Artery Bifurcation Stenosis and Ischemic Cerebrovascular Disease

Approximately 50,000 Canadians suffer an ischemic cerebrovascular event each year. It is thought that 30-50% of these ischemic events are secondary to embolic phenomena originating from the internal carotid artery bifurcation in the neck (66). The North American Symptomatic Carotid Endarterectomy Trial (NASCET) revealed an absolute risk reduction of stroke of 17% at 2 years after surgical treatment in patients with ischemic symptoms and at least a 70% diameter stenosis of the cervical carotid artery (58). Following this study current clinical guidelines suggest that patients found to have greater than 70% stenosis of the carotid artery will benefit from surgical intervention (carotid endarterectomy). As the degree of carotid stenosis is a major determinant of benefit from carotid endarterectomy an accurate assessment of the carotid

artery bifurcation is essential. The current investigation of choice is digital subtraction angiography (DSA). However new modalities are available (namely computed tomographic angiography (CTA)). This will be the focus of the present review.

Radiologic Investigation of Cerebrovascular Disease

A) Present Modality

Until now the radiologic procedure of choice for demonstrating intracranial aneurysms, cerebral vasospasm, and carotid artery bifurcation stenosis has been digital subtraction angiography (DSA) (fig. 1-4). This technique involves a catheter inserted over a guide wire into the femoral artery. A brief description of the technique is given here, and a more detailed description is found in reference 73. The catheter is passed retrograde from the femoral artery to the aortic arch. Using fluoroscopic x-ray technology the position of the catheter tip can be localized in the vessel lumen. After the catheter tip is positioned in the carotid arteries and vertebral arteries individually, a small volume of contrast media is injected into the lumen of the artery. The contrast media consists of an iodine-based, nonionic, water- soluble solution. The high density of the contrast media does not allow transmission of x-ray beams. Just before the contrast media is injected a x-ray picture of the region is taken. Once the contrast media is injected multiple serial x-ray pictures of the region are taken. An automated computer algorithm subtracts the initial x-ray picture from each of the pictures taken as the contrast was being infused. This results in an image of the contrast media in the artery lumen. Typically, pictures are taken in three viewing planes; posteroanterior, lateral, and oblique. Imaging of the intracranial arterial vasculature for diagnosis of aneurysms and vasospasm, and demonstration of carotid artery stenosis are accomplished through this technique.

Digital subtraction angiography is an invasive procedure and is therefore not without complications and risk to the patient. Complications can be divided into three categories; local, systemic, and neurologic.

i) Local Complications

These occur at the arterial puncture site and include hematoma, artery dissection, thrombosis, pseudoaneurysm formation, arteriovenous fistula, infection, and retroperitoneal hemorrhage. The overall incidence of these complications is 5-7%, with hematoma being the most common, representing approximately 80% of local complications (18, 92).

ii) Systemic Complications

These complications are due to the nonionic contrast media used. Complications included in this category include nausea, vomiting, allergic reactions (minor- itching, urticaria; major-hypotension, dyspnea), and renal impairment. The overall incidence of these reactions ranges from 1.8-3.2% (18, 92, 37). Nausea represents 30-50% of these complications. The incidence of serious complications (major allergic reaction, renal impairment) is about 0.05% (37).

iii) Neurological Complications

Very rare complications include transient global amnesia, cortical blindness, confusional states, and dementia (67). More common neurological complications include ischemic events that may be transient (duration < 24 hr), reversible (duration < 7 d), or permanent (duration > 7 d). The overall incidence of neurological complications has been reported to range from 1-4% (18, 91, 92, 25, 67). The vast majority are transient with a permanent neurologic deficit rate of 0.3-0.5%.

As outlined above DSA exams have significant risks associated with them. As technology advances newer modalities with comparable performance to DSA and with less risk to the patient are constantly explored. The next section reviews the more recent modalities used to investigate cerebral aneurysms and carotid artery stenosis.

B) Newer Modalities

1. CT Angiography

Recent advances in computed tomography (CT) have allowed the development of angiographic applications of this technology. In 1979 CT was invented by Hounsfield and Cormack. It consisted of a single x-ray source and detector mounted opposite to each other on a ring (55). The ring would rotate around the head at intervals of a few degrees

at a time, sending and detecting electron beams at each interval. Once a span of 180 degrees was accomplished the patient was moved several millimeters and the processed was repeated, this occurred over the desired scan volume. CT scanners utilize the same principles of other x-ray devices; x-rays are passed through the patient and detectors measure the degree of x-ray transmission through the patient. Tissues of differing densities will transmit the x-rays to a varying degree; more dense tissues will attenuate the x-rays more than less dense tissues. This initial first generation CT scanner was crude and excruciatingly slow. Since the first CT scanner there has been a continuing evolution in the scanner technology.

Present CT scanners have multiple detectors mounted around the scanner ring and a continuously rotating fan beam which reduces the scanning time to only seconds per section. The scanner is still limited in only being able to rotate through one complete rotation before having to reverse its direction and the patient needs to be moved after every rotation.

In order for the CT scanner to be useful in depicting contrast filled arteries it must be capable of rapid and continuous data acquisition. This follows from the fact that intra-arterial injection of contrast media will be quickly removed from the artery as blood flows from artery to vein. Previous generations of CT scanners were not optimal to capture the intra-arterial phase of contrast administration. The application of slip ring technology to CT scanners has permitted new generation spiral CT scanners to capture the arterial phase of contrast administration. This technology allows the scanner to continuously obtain data as the patient is translated through the scanner (fig.1-1). The end result is the volume of interest is scanned 5-10 times faster than with conventional scanners (55).

In performing CT angiography (CTA) the spiral CT scan must be acquired at the time of maximum concentration of contrast media in the arteries of concern. There are three main aspects factors that influence CTA quality; contrast bolus parameters, scanner parameters, and 3-D computer reconstruction of the source data (57).

i) Bolus Parameters

These include contrast bolus amount, injection rate, injection duration, and the delay between start of contrast media injection and the start of data acquisition (scanning). When contrast is injected through a peripheral vein it has to circulate through the right side of the heart and the lungs before it reaches the arterial vessels, this results in dilution and stretching of the bolus length and duration. It follows then that the amount, rate, and duration of the contrast bolus injection must be sufficient enough to overcome the circulation effects in order to result in a high concentration in the desired arteries. Previous reports have found bolus amounts of 90-120cc and injection rates of 2-3cc/sec to provide sufficient contrast enhancement of the arteries (57, 3, 14, 34). The delay from start of contrast injection to start of scanning is equal to the circulation time from the peripheral vein to the desired artery. This will depend on several factors; injection rate, central or peripheral vein, poor cardiac function, and lung function (75, 54). Patients with poor cardiac output (congestive heart failure) or lung function (asthma, COPD, chronic smoking) cause a thinning, lengthening, and slowing of the contrast bolus (57). When compared to normal patients these patients will have a longer delay from the start of injection to peak contrast enhancement, as well the peak contrast intensity will be lower for a given contrast amount and injection rate. Injection into a central vein will similarly result in a quicker time to peak enhancement, as well the magnitude of enhancement will be greater (54). This, again, follows from the fact that the more peripheral the vein the more the contrast will be diluted and lengthened before reaching the arterial vessels. Nakajima et al (54) also found that elderly age (>70 years) and higher grade of subarachnoid hemorrhage resulted in longer time to peak arterial enhancement. The delay time can be determined with a preliminary test dose involving a small volume of contrast (20cc) injected at 3cc/sec with the start of scanning at the appropriate level 8-10 sec later (49). Multiple scans are performed at the same level and a graph plotting time to contrast enhancement can be made (fig. 1-2). The time to peak enhancement on this graph is the scan delay for the formal CTA.

ii) Scanner Parameters

Not only does the contrast bolus need to be perfect, but there are certain scanner parameters that are important in obtaining a CT angiogram. These include the scan duration, the collimation width, and the table speed. These latter two parameters are

major determinants of optimum resolution of CTA. The collimation width is the width of the x-ray beam in each section of the scanned volume. Greater collimation widths result in a greater tissue volume exposed to the x-ray beam, this has been found to result in poorer resolution through partial volume errors, artifacts, and scatter (20, 33). The table speed is the speed through which the patient is translated through the scanner. Faster table speeds will result in a greater volume covered in less time, which favors minimizing venous enhancement, but at the expense of spatial resolution (49). Pitch is the ratio of table speed to collimation and can be thought of as the number of collimation widths covered in one gantry rotation (55). One study of the intracranial vessels found no difference in resolution between pitch=1 and pitch=1.5, however pitches greater than this resulted in decreasing spatial resolution (34). It has been previously reported that for intracranial vessels a collimation width of 1 mm and a table speed of 1 mm/sec (pitch=1), and for carotid arteries a collimation width of 2-3 mm and a table speed of 3 mm/sec (pitch=1-1.5) provide optimum resolution (49).

iii) 3-D Reconstruction

Once the CT scanner has finished scanning the desired volume a computer algorithm reconstructs the images into thinner, overlapping sections. Using the original data the scanner reconstructs, or creates, another slice based on the known original surrounding slices (55). The purpose of this is to increase spatial resolution and decrease partial volume effects inherent to CT scanning. The reconstructed images are overlapping which results in smoother 3-D reconstructions. The reconstructed images are then electronically transferred to a 3-D computer workstation. Two 3-D models are used; maximum intensity projection (MIP) and shaded surface display (SSD) (fig. 1-5).

a) Maximum Intensity Projection (MIP)

The basic tenet of the MIP algorithm is that the intensity of each pixel in a MIP image is the maximum intensity encountered along each ray from a single viewpoint (57). MIP images are displayed in the Hounsfield grey scale of conventional CT scans thus tissues of high density such as bone will be displayed as well as the contrast media in the blood vessels. At times the bone can obscure the vascular structures, therefore editing techniques must be employed to remove all extraneous tissue other than the contrast filled vessels. There are two main editing techniques; manual or automatic editing. With

manual editing extraneous tissues such as bone are removed with an electronic scalpel. The automatic editing technique involves removal of certain tissues according to a desired Hounsfield level (measure of intensity). In CT imaging all tissues have a certain density or Hounsfield unit (bone is very high, air is very low) and thus by selecting a certain Hounsfield level tissues of that density can be removed.

There are a variety of drawbacks of MIP images. As MIP images present only the pixel with maximum intensity there is loss of data, this results in an increase in noise, however this increase in noise is compensated for by an increase in the contrast-to-noise ratio (57). MIP images lack depth and thus the relative positioning of overlapping vessels cannot be determined without rotating the image. Slices acquired later in the scan will have more parenchymal and venous enhancement and therefore contrast between the vessel and the surrounding tissue will be less than in earlier slices. Venous enhancement may be difficult to separate from the desired artery especially in the area of the cavernous sinus.

b) Shaded Surface Display (SSD)

The SSD algorithm takes the reconstructed images provided by the spiral CT scanner and computes a mathematical model of a surface that connects neighboring pixels with CT densities above a preset threshold (Hounsfield unit) (57). Then, for a given view direction, an image is created that shades the surface in proportion to the amount of light it would reflect from a simulated light source back to the observer. SSD images do not preserve the Hounsfield grey scale, thus all structures are given the same intensity but are shaded according to their position in the image to give the perception of depth. SSD images do retain depth-dependent cues which are lost in MIP images.

The major drawback of SSD images is the image is dependent on a preset threshold level (57). A choice of too low of threshold will result in more information (eg. venous or parenchymal structures, or underestimation of stenosis) being included in the SSD image. Too high of a threshold will result in less data being included in the SSD image eg. less intensely enhanced vessels will be lost, stenosis may be exaggerated.

Advantages of CTA Compared to DSA

In general, there are several advantages of CTA compared to DSA (57). With a single contrast injection an entire volume can be acquired by CTA and the resultant 3-D images can be displayed from any vantage point, whereas typically DSA provides 3 views and any further views require extra contrast injection. An arterial puncture is performed with DSA requiring bed rest and nursing observation for 4-6 hr, with CTA only a venous puncture is made and post procedure observation and bed rest are not required. The local and neurologic complications of DSA outlined in the previous section do not occur with CTA. Complications associated with CTA are secondary to contrast media administration, and slightly higher than with DSA due to venous rather than arterial contrast injection. Digital subtraction angiography produces 2-D images and thus overlapping vessels may obscure precise delineation of the anatomy. With CTA the images can be edited to remove overlying structures. The images can also be rotated in any plane for precise visualization. Conventional angiography is an intraluminal technique and as such does not give any information about soft tissues such as mural abnormalities. Soft tissue discrimination is preserved with CTA thus mural thrombus and calcifications are displayed. The cost of CTA has been estimated to be 31% of the cost of DSA (22).

Disadvantages of CTA as Compared to DSA

In general, DSA is thought to be superior in spatial resolution (57). The high contrast-to-noise ratio of DSA is superior to CTA. There is no temporal resolution with CTA, an important advantage of DSA. With DSA more than one arterial site can be examined at the same sitting eg. cerebral, carotid, and aortic arteries can be visualized at the same time whereas CTA only visualizes one arterial site at a time eg. cerebral vessels or carotid vessels. Another disadvantage of CTA is the operator dependence of the 3-D computer processing which depending on the experience of the person performing the processing the quality of the 3-D images may differ (7). The 3-D computer processing is also time consuming even in experienced hands (57). Disadvantages, and advantages, specific to cerebral aneurysm detection, cerebral vasospasm detection, and carotid artery stenosis will be addressed respectively in the following sections.

2) Ultrasonography

Doppler ultrasonography (US) is a noninvasive modality in which an ultrasound probe sends and receives ultrasonic waves directed at column of flowing fluid. The velocity of the fluid can be determined by the Doppler effect and from this information the relative diameter of the vessel through which the fluid is moving ca be determined. This technology has been applied to the carotid artery bifurcation to detect stenosis, or narrowing, of the internal carotid artery. There have been several previous reports comparing US with DSA in detecting carotid artery stenosis (5, 19, 26, 28, 53, 64, 72, 77, 80, 81). Ultrasound has been found to be highly sensitive (92%) for complete occlusions (77) and for detecting >50% carotid artery stenosis (90-100%)(77, 81). In detecting moderate stenosis (40-70%) US has been reported to be less sensitive (63-69%) (77, 81). There have been a few studies examining the ability of US to detect 70-99% carotid stenosis. They report sensitivities and specificities ranging from 81-94% and 83-98%, respectively (19, 26, 53, 64, 72).

US has significant advantages over DSA. It is a non-invasive exam, therefore the local, systemic, and neurological complications of intra-arterial catheterization are avoided. US does not have the complications of the intravascular contrast injection. The cost is less, accessibility is greater, and US typically does not require as great a time commitment as DSA.

There are certain disadvantages of US that limit its ability to replace DSA for investigating carotid artery disease. As the above review of the literature reveals, US is not perfect in detecting all degrees of stenosis, as compared to DSA. A significant problem with US is its high variability. Multiple authors have previously reported a high interobserver and intermachine variability (28, 72). The less than perfect sensitivity and high variability have made US a screening only modality at present.

CT Angiography for the Detection of Cerebral Aneurysms

Digital subtraction angiography (DSA) is the current gold standard for the diagnosis of intracerebral aneurysms, therefore any new investigative modality must be

comparable to this standard. Computed tomographic angiography (CTA) has been recently introduced and is a potential replacement for DSA for the diagnosis of intracranial aneurysms. Table 1-1 provides a summary of the major previous studies.

1) Sensitivity of CTA as Compared to DSA

Aoki et al (3) first reported their experience with CTA in demonstrating cerebral aneurysms and compared it to DSA. In their study of 15 patients, 2 of which had sustained a subarachnoid hemorrhage, a sensitivity of 100% was reported. The smallest aneurysm in their study was 3mm. Two years later Schwartz et al (70) reported their series of 21 patients, with 7 patients sustaining a subarachnoid hemorrhage. This was the most reported SAH patients to date, and they found a sensitivity of CTA, as compared to DSA, in aneurysm detection of 87%. They found that aneurysms 2mm in size were not detected by CTA and that aneurysms close to the skull base (internal carotid artery aneurysms) were difficult to see on 3-D reconstructions. Source axial images were more useful. Another significant result from this study was that subarachnoid blood was thought to obscure some aneurysms. This may be explained by the relatively low contrast amount (75cc) injected. This results in less enhancement of the arterial vessels. Enthusiasm for CTA in detecting aneurysms continued after these initial reports and the largest series to date of subarachnoid hemorrhage patients was reported by Vieco et al (90). In their series of 30 patients, utilizing one CTA experienced reviewer and one inexperienced reviewer, sensitivity of CTA in aneurysm detection was 97% and 77%, respectively. The smallest aneurysm in this series was 4mm. They found that CTA correlated well with DSA in aneurysm size and that subarachnoid blood did not affect the quality of the images.

As interest grew in CTA it became more widely investigated which reflected increasing sample sizes in the literature. Alberico et al (2) in 1995 reported the largest series, at the time, comparing CTA to DSA for cerebral aneurysms. A total of 68 patients were studied, 23 having sustained a subarachnoid hemorrhage. They had three reviewers ranging from very CTA experienced to CTA inexperienced, with reported sensitivities of 95%, 90%, and 85%, respectively. The smallest aneurysm in this study was 2mm, and there were five such aneurysms. In this series all posterior communicating artery

aneurysms, 2 of which were 2mm in size, were undetected by CTA. They did not find subarachnoid blood to have any effect on the CTA images. Hope et al (27) reported in a series of 80 patients being investigated for a cerebral aneurysm differing sensitivities depending on the size of aneurysm. The overall sensitivity of CTA, as compared to DSA, was 90%, however, the sensitivity for aneurysms > 11mm in size was 100%, and that for aneurysms < 3mm was 64%. They concluded the resolution of CTA may be limited by the size of the aneurysm.

A more recent study of 53 SAH patients revealed a sensitivity for CTA of 98% with only a 3mm posterior communicating artery aneurysm not detected by CTA (42). A similarly recent series of 80 SAH patients reported a sensitivity of 88%. In 83% of cases in which CTA and DSA were in agreement it was thought that CTA was superior to DSA in the depiction of the aneurysm (88). In this study poor quality of the CTA images was the most common reason for CTA missing aneurysms. All of the missed aneurysms in this study were less than 5mm in size and were located on the internal carotid artery.

Ng et al (59), in their series of 26 patients (21 SAH), reported one missed aneurysm by CTA (posterior communicating artery aneurysm), but also reported inaccuracies with DSA. They found that there were 3 aneurysms missed by DSA, but seen on CTA and confirmed intraoperatively. They also found 2 false positive results with DSA, where CTA was negative, and the initial DSA was reported to be positive. However, after extra DSA views were performed the structures thought to be aneurysms were kinked and overlapping vessels. The largest study to date of CTA detection of aneurysms in the setting of acute subarachnoid hemorrhage is by Zouaoui et al (100). They report 120 SAH patients who underwent CTA and DSA (80 preoperatively and 40 postoperatively). The aneurysm size in this series ranged from 2mm-35mm and the sensitivity of CTA for aneurysm detection was 97%. They, like Ng et al (59), reported 2 cases in which CTA was positive for a middle cerebral artery aneurysm, DSA was negative, and intraoperative exploration confirmed the aneurysms depicted by CTA. These two studies suggest that even the present gold standard is not 100% sensitive in detecting aneurysms. Other than confirmation by autopsy, DSA remains the test to which all newer tests must be compared.

2) Specificity of CTA as Compared to DSA

Not only is sensitivity important when comparing two tests, but also specificity. Concluding that an aneurysm is present when it is not can lead to inappropriate treatment (surgery) with its inherent risks. One of the earliest studies comparing CTA to DSA in aneurysm detection reported a specificity of 93% (3). In that series a branching vessel was interpreted as an aneurysm. This was said to be due to the poorer resolution of CTA for small vessels. Since then several studies have investigated CTA and DSA for aneurysm detection and have reported specificities of 100% (70, 90, 2, 100, 42, 89). In the studies that did not report a specificity of 100% the range in these studies was 77%-93% (90, 2, 43, 29, 59, 88, 89). The false positive CTA's tended to occur with less experienced reviewers (89, 90, 2). The false "aneurysms" were more commonly located on the internal carotid artery (43, 2, 90, 88) and anterior communicating complex (59).

Hope et al (27) reported a specificity of 50%, much lower than the rest of the literature. They report that 93% of these false aneurysms were < 3mm in size, and 36% were located on the internal carotid artery, and 59% were located on the middle cerebral artery. They conclude that the high number of false positive CTA's was due to erring on a higher index of suspicion rather than on a lower index as this would result in a higher false negative rate. The low level of specificity in this study was more likely attributable to a relative inexperience of the reviewers with CTA.

3) MIP vs. SSD Images

The general advantages and disadvantages of MIP and SSD images was discussed in a previous section. Review of the literature comparing CTA to DSA for the detection of cerebral aneurysms produces differing opinions on the relative value of these two imaging techniques. Various authors (88, 89, 100) advocate the use of MIP images over SSD images as they are threshold independent, less dependent on the user (100), and are thought to show distal arterial branches better than SSD images (27). Velthuis et al (89) compared MIP and SSD images for detection and demonstration of the aneurysm complex and concluded MIP images to be superior despite being more time consuming to produce and lacked depth.

Other investigators (17, 90, 43) report SSD images to be superior to MIP images. These images are quicker to produce, have depth cues, show the relationship of the vessels to bone, and the bones of the skull base obscure the vasculature less.

A compromise is provided by Ng et al (59). They advocate using both imaging methods as they compliment each other. The combination provides more information and fascilitates appropriate clinical decision making.

4) Pitfalls of CTA and Diagnosis of Cerebral Aneurysms

Review of the literature reveals that CTA may fall short of DSA in detecting aneurysms because of the following factors;

i) *Aneurysm Size:* Initial studies reported difficulty of CTA in detecting small aneurysms (<3mm) (70). A later study (2) also showed poor detection of 2mm aneurysms. Hope et al (27) reported a sensitivity of 100% for aneurysms > 11mm, but aneurysms < 3mm had a sensitivity of only 64%. Ogawa et al (61) published even poorer sensitivity for aneurysms 2-4mm in size (19-24%). In Velthuis et al (88) all of the false negative CTA's were for aneurysms of <5mm in size. Tampieri et al (84) reported a sensitivity of 50% for aneurysms < 3mm in size. Review of the literature suggests that although the exact sensitivity of CTA in detecting small aneurysms (<4mm) is variable, it appears to be less than for larger aneurysms.

ii) *Aneurysm Location:* In his initial report Aoki (3) stated that posterior communicating artery (p-comm) aneurysms were more difficult to detect by CTA. Vieco et al (90) concluded that aneurysms near the skull base (internal carotid artery aneurysms) were more difficult to detect especially in less experienced hands. Alberico et al (2) also reported p-comm aneurysms to be difficult to detect in their series as this type of aneurysm was missed by CTA. Both of the false negative CTA's in Liang's (43) series were of the internal carotid artery. Ogawa et al (61) concluded that the intracavernous internal carotid artery was not displayed well by CTA.

Wilm's et al (96) reported even larger (5-8mm) p-comm aneurysms were difficult to delineate clearly by CTA. In a comparison of the quality of aneurysm display between CTA and DSA it was reported that 63% of internal carotid aneurysms were inferior with CTA. Velthuis et al (88) echoed others in that all of their false negative CTA's were of the internal carotid artery. It appears from the literature that aneurysms of the internal carotid artery are more difficult than other sites to detect, and accurately depict on CTA.

iii) *Bone Editing:* The bones of the skull base obscure visualization of the vessels near the base of the skull (internal carotid artery) to a significant degree, especially on MIP images (70, 90). In order for adequate visualization time consuming bone removal must be performed, and even after editing the images may not be optimal. It follows then that aneurysms near the skull base may be difficult to clearly identify.

iv) *Learning Curve:* As with all new procedures there is a learning curve to CT angiography. Napel et al (56) stressed the importance of proper bolus timing. The processing and interpretation of CTA images also has a steep learning curve. This is evidenced by a few studies that have reported that the sensitivity and specificity for aneurysm detection by CTA, as compared to DSA, improves as the reviewer becomes more experienced with CTA technology (90, 2, 23).

v) *Time Constraints:* SSD images can be produced in 2 minutes (43) to 8 minutes (90), however MIP images are reported to take longer as bone removal must be performed. Reported times for MIP images ranges from 30 minutes (3) to 60 minutes (70). This is a function of both computer software capabilities as well as reviewer experience. More recent studies quote processing times of only 15 minutes (88).

CT Angiography for the Detection of Cerebral Vasospasm

Cerebral vasospasm after subarachnoid hemorrhage is a significant cause of morbidity and mortality as outlined in a previous section. The present gold standard for diagnosis of vasospasm is digital subtraction angiography. The advent of CTA and its excellent display of the intracranial vasculature, coupled with its lower patient risk make it a natural choice for use in vasospasm. To date, there have been sparse previous reports of CTA use in the setting of vasospasm. The first report dedicated to CTA diagnosis of vasospasm, compared to DSA, was by Ochi et al (60). This study consisted of two patients who underwent CTA 12-13 days post subarachnoid hemorrhage. The patients had also had DSA performed 10-11 days post hemorrhage. Comparison of the CTA and DSA exams showed similar results, however the vasospasm was less precisely depicted by CTA than DSA due to the poorer resolution of CTA.

Since that initial report by Ochi (60), there have been anecdotal reports in a few other studies of CTA in the setting of acute subarachnoid hemorrhage. Zaououi et al (100) mentioned 5 cases in which CTA showed vasospasm comparable to DSA, in their series of 120 SAH patients. Van Loon et al (87) in their series of CTA performed postoperatively in 11 patients reported 3 cases in which CTA depicted vasospasm. Similarly, Velthuis et al (88) reported 3 cases of CTA depicting vasospasm in their series of 80 patients. There has not been a large series to date exclusively examining the utility of CTA in detecting vasospasm, as compared to DSA. These preliminary case reports are promising, however larger series are needed to fully evaluate the role of CTA in detecting cerebral vasospasm.

CT Angiography for the Diagnosis of Carotid Artery Stenosis

1) Agreement Between CTA and DSA

In comparing CTA to DSA for the detection of carotid artery stenosis the degree of correlation between the two tests needs to be assessed. Clinically, the North American Symptomatic Carotid Endarterectomy Trial (NASCET) looked at the degree of carotid bifurcation stenosis and the benefit of medical versus surgical therapy (58). They found

that patients with 70-99% stenosis benefited from surgery. In the NASCET study the degree of stenosis was classified as none, mild (<30%), moderate (31-69%), severe (70-99%), and occluded. This is the classification used by almost all investigators comparing CTA to DSA for carotid stenosis.

Schwartz et al (71) provided one of the first studies comparing spiral CTA with DSA. In their series of 40 arteries they reported an overall agreement of 92% between CTA and DSA, with perfect correlation in all degrees of stenosis except in the mild category (79%). Marks et al (50) had similar results in a series of 28 arteries. Their overall rate of agreement was 89% with perfect correlation in severely stenosed lesions and 86% in mild to moderate stenosis.

Still relatively early in the reports of comparing CTA to DSA Castillo (9) showed only an overall agreement of 50%. In this series CTA tended to overestimate the degree of stenosis with 6 arteries reported as occluded when they were actually severely stenosed. His discrepant results were likely secondary to technique as only 60cc of contrast was used, and collimation width was 5mm. This differs from most investigators, in that a contrast bolus of about 100cc is common and a collimation width of at least 3mm is required for adequate resolution.

The early encouraging reports of the potential use of CTA in carotid stenosis resulted in more widespread experimenting with CTA. Link et al (45) presented their large series of 92 arteries with an overall agreement of 85%. They found CTA underestimated the degree of stenosis especially in the presence of calcification. Agreement for mild, moderate, severe, and occluded vessels was 59%, 82%, 90%, and 100% respectively. His follow up series of 56 arteries (46) showed improved results with increased experience. Agreement between CTA and DSA was overall (89%), mild (73%), moderate (75%), severe (100%), and occluded (100%).

More recently, Simeone et al (76), in a study of 80 arteries, reported an overall agreement of 94%. This series however, had only 25 of the 80 vessels positive for any degree of stenosis, so the abundance of normal arteries blunt their excellent results. Another very recent study by Magarelli et al (48) revealed a concordance rate of 88% and accuracy of 91%. They also reported that CTA tended to underestimate the degree of

stenosis. For severely stenosed and occluded arteries their agreement rate was 92% and 100%, respectively.

In summary, CTA has demonstrated a high overall concordance with DSA in detecting carotid artery stenosis (Table 1-2). The high rate of concordance appears to translate to the severely stenosed and occluded artery categories. To date, most of the studies have reported relatively poor concordance between CTA and DSA for mildly stenosed arteries. The reports also appear to be consistent with CTA, in general, underestimating the degree of stenosis, as compared to DSA.

2) Axial vs. MIP vs. SSD Images

Review of the literature regarding the relative value of axial, MIP, and SSD images reveals differing conclusions on which is of most use. Most studies advocate the use of MIP images over SSD images (50, 9, 12, 41, 45, 46, 6, 76, 82). An important advantage of MIP over SSD is that it is less operator dependent. Difficulties found with SSD images include a high rate of underestimation of the stenosis (44, 46), and dependence on a predetermined threshold level (too low level widens the vessels). There have been a few studies to date comparing these various imaging techniques. Leclerc et al (41) compared axial, MIP, and SSD images in 40 arteries. They found the concordance rate to be 95%, 96%, and 89% respectively. They concluded that the axial images were the best and that MIP images were also very good. However, in the presence of calcification MIP images were less useful (10 arteries were not assessable on MIP or SSD images due to calcification). They, and others (63), concluded that SSD images always underestimated the degree of stenosis. Tarjan et al (86) also compared axial, MIP, and SSD images in 30 arteries. They reported agreement rates of 97%, 66%, and 59%, respectively. They echoed Leclerc's (41) conclusions: MIP and SSD images were poor in the presence of calcification, but their agreement increased to 83% once the calcium was removed. In a controlled phantom model Dix et al (16) concluded axial images to be the most concordant with DSA.

After review of the literature it appears that CTA most closely agrees with DSA when axial images are used for stenosis measurement. MIP images are also good, if

calcification can be completely removed. Despite the ease and quickness of SSD images they do not appear to be the best image to determine degree of stenosis.

3) Pitfalls of CTA in Carotid Stenosis

i) *Time Constraints:* Most authors report a processing time of about 15-30 minutes (71, 9, 12, 15). This time is generally doubled if there is heavy calcification present (41, 48). More recent reports have described processing times of 10 minutes (41), most likely as a result of powerful computer workstations and greater operator experience.

ii) *Calcification:* Calcification of the carotid artery bifurcation presents a major difficulty in depicting stenotic lesions. The incidence of calcification ranges from 11%-78% (50, 44, 45). Calcification results in underestimation of the degree of stenosis on SSD images (46), increased processing times (48), and partial volume averaging effects on the stenotic segment (83). It has been advocated that in the presence of calcification stenosis measurements should be made from axial images (6).

iii) *Ulcers:* The presence of ulceration in the plaque has been reported to be well demonstrated by CTA, especially large ulcers (71, 12, 15).

iv) *Tandem Lesions:* CTA only examines the cervical carotid artery therefore more proximal vessels (aortic arch) and more distal vessels (carotid siphon, intracranial vessels) are not visualized. Thus carotid siphon stenosis may be missed if only CTA is performed. The importance of these distal stenoses is questionable and recent studies report their presence has no effect on surgical treatment of the carotid bifurcation (69, 51, 47). Intracranial vascular abnormalities will also be missed by CTA. Aneurysms are the most frequent intracranial vascular abnormalities (1-5% incidence).

v) *Technical Parameters:* There have been multiple studies using phantom models to examine the impact of various technical factors of CTA in the quality of CTA (13, 98, 16, 11, 97, 79, 10). The conclusions drawn from

these studies include: (1) the narrowest collimation width should be used (2-3mm), (2) the pitch should be increased preferentially over the collimation width and (3) image degradation starts to occur with pitch > 2:1. Vessels that are parallel to the table movement have the least degradation. Shorter stenotic segments (<2mm) have more partial volume averaging artifact and image degradation.

Other Applications of CT Angiography

CT angiography has not only been studied for the detection of cerebral aneurysms and carotid stenosis, but also in the diagnosis of pulmonary artery embolism, coronary artery thrombosis, renal vasculature, and for abdominal aortic aneurysms (75, 99). Neurological applications include intracranial venous anatomy, cerebral artery thrombosis, arteriovenous malformations, and most recently endovascular CTA techniques.

i) *Venous Anatomy:* Konno et al (40) reported a case study of a neonate with a vein of Galen aneurysm. They found CTA, especially SSD images, to be of significant value in showing direct fistulous communications arteries and veins. Casey et al (8) performed 36 CT venograms, 21 for suspected dural sinus thrombosis and 12 for tumors in close relation to the sinuses. They reported perfect correlation of CTV, as compared to MRA, in depicting dural sinus thrombosis. They concluded that CTV was easier, quicker, and had less artifact than MR venography. In a study of 4 cases Peebles et al (65) were able to show developmental venous anomalies with CTV. They were able to demonstrate small deep vascular structures converging on dilated superficial veins.

ii) *Cerebral Thrombosis:* With the established role of thrombolysis in acute ischemic stroke, rapid diagnosis of cerebral thrombosis is required. One of the attractive features of CTA is that it can be performed immediately following plain CT of the head, therefore it would be of great use in

thrombolysis if it can accurately diagnose cerebral thrombosis. This has led to a few studies evaluating the ability to detect arterial thrombosis. Shrier et al (74) reported, in a series of 28 patients, a 99% overall agreement of CTA with DSA in depicting thrombosis. Their sensitivity, specificity, and accuracy of CTA were 89%, 100%, and 99%, respectively. Knauth et al (39) reported their experience with 21 patients. Only 11 of these had a DSA to compare the CTA to. In these eleven cases they reported perfect agreement in depicting thrombosis. A later study by Hunter et al (30) compared CTA with perfused blood volume in acute stroke. Their results were less convincing with 6 of 13 patients in agreement, however 7 of the 13 patients with a perfused blood volume deficit did not have a corresponding defect on CTA. The studies to date evaluating the use of CTA in acute stroke are encouraging, however there has not been a proper study of a large number of patients undergoing both CTA and DSA. Until such a study is done, one cannot assume CTA has a definitive role in diagnosing acute cerebral thrombosis.

iii) *Arteriovenous Malformations:* Harbaugh et al (22) presented one case study of CTA for AVM's. This patient had a large AVM with a gigantic varix draining to the vein of Galen. CTA delineated the relationship of the nidus to the draining varix and to surrounding vessels and skull base. It was concluded that CTA gave a better appreciation of the anatomy due to its ability to view the lesion from all directions. Rieger et al (68) reported their experience with CTA in 13 AVM patients. They claimed the main feeding arteries as well as the dilated draining pial veins were identified in all cases. The AVM nidus was reliably depicted. More recently Tanaka et al (85) performed CTA and DSA in 12 patients with AVM's. Their results were less impressive with only 50% of feeding arteries, and 78% of draining veins demonstrated by CTA. Nidus measurement was possible in all patients. Heffez et al (24), in 19 AVM patients found CTA to be helpful for surgical planning in 68% of patients. To date, there has not been a large enough study to define CTA's role in AVM's. It is likely, due

to the complex anatomy of AVM's, to be adjunctive to DSA rather than replace DSA in the diagnosis of AVM's.

iv) *CTA Endoscopy:* With newer, more powerful software packages being produced the capability of endoscopic applications of CTA are now possible. Aneurysm characteristics such as intraluminal thrombus, calcification, and orifice detail can be clearly revealed with CTA endoscopy (38). Kato et al (38) conclude that CTA endoscopy will be useful in situations where the aneurysm neck may not be clearly visualized or where there are early arterial branches from the neck or dome of the aneurysm.

Conclusions

1) CTA for Cerebral Aneurysm Detection

As presented in previous sections, there are numerous studies comparing CTA to DSA for the detection of intracranial aneurysms. Most of the early studies concentrated on nonhemorrhage patients, but more recent papers have addressed CTA's use in the setting of subarachnoid hemorrhage. The overall consensus of these reports is that CTA appears to have a high sensitivity and specificity for aneurysm detection, when compared to DSA. Early it was suggested that CTA may not be as useful for aneurysms of < 4mm in size, but more recent studies question this. The purpose then, of conducting another study comparing CTA to DSA for aneurysm detection is multiple. First, CTA needs to be introduced to the present institution and a valid protocol needs to be developed. Second, after developing a protocol for CTA it needs to be performed in a large number of patients to replicate previous authors' experiences. Third, CTA must be validated for use in acute subarachnoid hemorrhage at this institution. Finally, the sensitivity of CTA in detecting small aneurysms needs to be fully evaluated, as this is still unresolved in the literature.

2) CTA for Cerebral Vasospasm

Cerebral vasospasm is a relatively common occurrence after subarachnoid hemorrhage. The present standard is to use DSA for diagnosis. However the preliminary encouraging results of CTA in detecting intracranial aneurysms suggests that CTA also may be useful in detecting vasospasm. As reviewed in a previous section, the literature to date, examining CTA in the setting of vasospasm, is very limited. The few publications that are available are for the most part case reports. Preliminary results suggest CTA shows promise in detecting vasospasm. The purpose of this study is to perform a formal, large, prospective series to adequately assess CTA's ability to accurately detect cerebral vasopasm.

3) CTA for Carotid Stenosis

A comparison of CTA and DSA for the detection of carotid artery stenosis has been performed previously by several authors. They have shown that CTA has a high overall agreement with DSA with a high rate of concordance for severe stenosis and occluded vessels, but a lower concordance for mildly stenosed arteries. It is generally thought that CTA underestimates the degree of stenosis. There is less agreement in the literature regarding the optimum CTA image type, as some advocate SSD images, some MIP images, and some MIP and axial images. The rationale for performing another study comparing CTA to DSA for carotid stenosis is as follows. First, the development of a CTA protocol for carotid stenosis needs to be made at this institution, where CTA for carotid disease has not been previously performed. Second, the replicability of previous results needs to be evaluated. Finally, one purpose is to formally compare the utility of each of the CTA image types (axial, SSD, MIP) in accurately diagnosing carotid stenosis, as compared to DSA.

Table 1-1: Summary of Previous Studies Comparing CTA to DSA for Intracranial Aneurysm Detection

STUDY	TOTAL PATIENTS (SAH PATIENTS)	SENSITIVITY %	SPECIFICITY %
Aoki et al (3)	15 (2)	100	93
Schwartz et al (70)	21 (7)	87	100
Vieco et al (90)	30	97, 77 (1)	100
Alberico et al (2)	68 (23)	95, 90, 85 (2)	100
Hope et al (27)	80	90 (3)	50
Lenhart et al (42)	53 (53)	98	100
Velthuis et al (88)	80 (80)	88	93
Zouaoui et al (100)	120 (120)	97	100

SAH =subarachnoid hemorrhage

(1): 97% for an experienced reviewer, 77% for an inexperienced reviewer

(2): 95%-experienced reviewer, 90%-moderately experienced reviewer, 85%-inexperienced reviewer

(3): 100% for aneurysms>11mm, 64% for aneurysms<3mm

Table 1-2: Previous Studies Comparing CTA to DSA for Carotid Stenosis Reporting Agreement Between CTA and DSA for Degree of Stenosis

	AGREE. BETWEEN CTA AND DSA					
STUDY	**OVERALL**	**MILD STENOSIS**	**MOD. STENOSIS**	**SEV. STENOSIS**	**OCCLUDED**	**N**
Schwartz et al (71)	92%	79%	100%	100%	100%	40
Castillo et al (9)	50%	NR	NR	NR	NR	20
Link et al (45)	85%	59%	82%	90%	100%	92
Link et al (46)	89%	73%	75%	100%	100%	56
Simeone et al (76)	94%	50%	50%	92%	100%	80
Magarelli et al (48)	88%	20%	50%	92%	100%	40

mod.=moderate, sev.=severe, N=total number of carotid arteries

NR=not reported

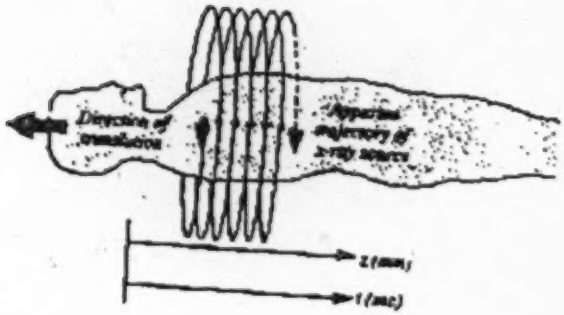


Figure 1-1. Spiral CT data acquisition geometry

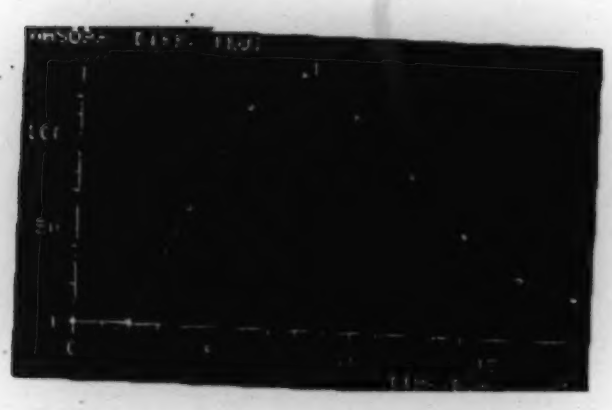


Figure 1-2. Time-density curve for determining peak arterial enhancement and proper scan delay.

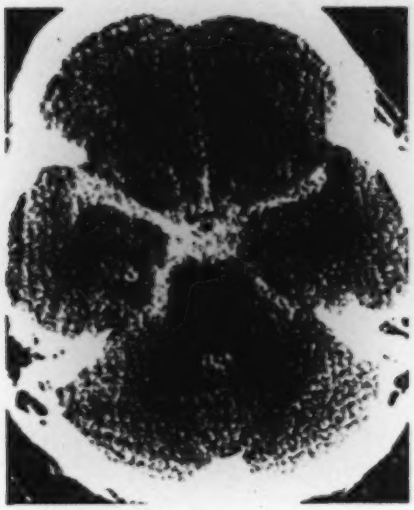


Figure 1-3. CT scan of the head showing subarachnoid hemorrhage (SAH)

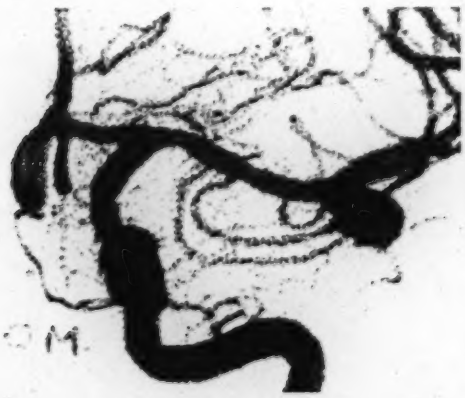
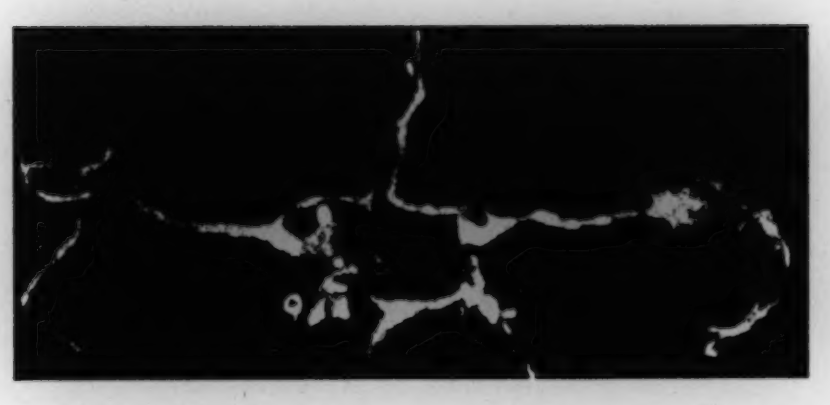


Figure 1-4. Digital subtraction angiogram (DSA) of the internal carotid artery.

A.



B.

Figure 1-5. CT angiogram (CTA) of the cerebral arteries. A-SSD, B-MIP.

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CT Angiography for the Detection of Intracranial Aneurysms in the Setting of Acute Subarachnoid Hemorrhage[1]

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Introduction

The advent of spiral computed tomography has led to the development of computed tomographic angiography (CTA), a technique that allows imaging of the intracranial arteries after an intravenous bolus administration of contrast material and rapid sequence CT-scanning (3,4,9,10). Less invasive and safer than digital subtraction angiography (DSA), where individual arteries are catheterized and injected with contrast solution, reports to date have also suggested that CTA is useful in providing additional anatomical definition of selected cerebral aneurysms(1,6). We developed a protocol to perform CTA of the circle of Willis for patients with suspected aneurysms, and we were particularly interested in the detection of aneurysms following acute subarachnoid hemorrhage (SAH). Since CTA has already been introduced as a technique, the primary objective of this study was to objectively compare anatomical information provided by CTA to the results of DSA.

Methods

Computed tomographic angiography was introduced to our hospital in July 1996, and between that time and October 1996, 40 consecutive patients with suspected intracranial aneurysms were examined by both CTA and DSA. Acute SAH was the presentation of 32 of these patients. Four other patients underwent CTA to rule out familial aneurysms, one patient with Ehlers-Danlos syndrome was screened for the presence of aneurysms, one patient was examined following aneurysm clipping to rule out multiple aneurysms, and two patients were investigated because of headache in the absence of CT evidence for intracranial bleeding. All patients in the series also

underwent DSA within several hours of the CTA study.

A General Electric Hi-Speed Spiral CT scanner is used for CTA at our institution, and images are processed with the General Electric Advantage Windows 3-D workstation (General Electric, Milwaukee, Wisc.). Digital subtraction angiography is performed using the Seldinger technique with femoral puncture and selective 4-vessel cerebral catheterization, obtaining anteroposterior, lateral, and oblique images.

The protocol for CTA developed at our institution consists of an initial test injection and scan to determine the circulation time from the contrast bolus injected in an antecubital vein to peak enhancement of the cavernous carotid artery. Optiray 320 (Mallinkrodt Medical, Pointe Claire, Quebec) is injected at 3 cc/sec for a total of 20 cc and 10 scans are performed at the level of the mid-sella turcica after a 10 sec delay. A graph is constructed of intensity (in Hounsfield units) over time with the region of interest being the carotid artery. Once the peak intensity is determined, 2 sec is subtracted from this peak and the resultant time is used as the scan delay for the CTA study.

In our experience middle-aged patients without significant cardiopulmonary disease reach maximum cavernous carotid enhancement in roughly 17 sec, so a scan-delay of 15 sec is used for CTA. Younger patients usually require a shorter scan-delay time between 10-12 sec, and older patients and those with significant cardiopulmonary disease generally require longer scan-delay times, between 20-25 sec.

Following this test injection the formal CTA consists of 100 cc of Optiray 320 injected at a rate of 3 cc/sec, and CT scanning commences after the aforementioned scan-delay. The volume scanned spans from the sella floor to 36 mm above the sella floor.

The collimation width of 1 mm, 1:1 pitch, 20 cm field of view, 120 KV, and 280-300 mA are used. The axial source images are immediately reconstructed to overlapping 0.5 mm sections for increased resolution.

The reconstructed images were then processed at the workstation into both shaded surface display (SSD) and maximum intensity projection (MIP) images of the cerebral arteries. Maximum intensity projection images underwent bone removal through thresholding and manual editing techniques. Shaded surface images were constructed using a threshold level resulting in maximal vascular detail, generally 100-130 HU. Images were pictured at 15° intervals covering 180° in two planes. The total time required for processing was 10-15 min, and is performed by the scanner technician with either a neurosurgeon or neuroradiologist to provide editing assistance.

The CTAs and DSAs were interpreted, separately and in a blinded fashion, by a neuroradiologist for presence, location, size, shape, lobularity, neck size, and relationship to adjacent arterial branches.

Results

Among the 40 patients in this series a total of 43 aneurysms were detected by DSA, 37 of which were seen on CTA. Of the 6 aneurysms seen on DSA but not CTA (false negative CTAs), 2 were located in the posterior fossa not routinely examined in this series, and the other 4 were anterior circulation aneurysms 3 mm or less in diameter as determined by DSA (table 2-1).

Ten patients had no aneurysm on DSA and 9 of these also had negative CTAs, the remaining patient (false positive CTA) was thought to have a 2 mm middle cerebral

artery (MCA) aneurysm based on CTA.

The overall sensitivity and specificity of CTA for the detection of aneurysm presence in this series was 86% and 90%, respectively. The size of aneurysms revealed by CTA ranged from 2 mm to 20 mm. Of those aneurysms 3 mm or less in diameter revealed by DSA, CTA was positive in 4 of 7 cases (57%).

Location, size and lobularity of aneurysms detected by CTA corresponded very well with the DSA images. CTA always detected the correct aneurysm location, and size estimates (table 2-2) equaled those provided by DSA. The aneurysm neck size (table 2-3) and number of aneurysm lobes present (table 2-4) also correlated well with DSA (figure 2-1) with accuracies of 97% and 95%, respectively. However, in one notable case the DSA was interpreted to have a single-lobed aneurysm, but CTA clearly showed a bilobed aneurysm to the extent it was almost two separate aneurysms (figure 2-2), and this morphology was confirmed at surgery.

CTA accurately determined the number of major branches near the aneurysm origin (table 2-5), an important consideration for middle cerebral artery aneurysm assessment (figure 2-3). For anterior communicating artery (ACommA) aneurysms, we found that the combination of aneurysm neck location, direction of aneurysm projection, and relative size of the proximal anterior cerebral arteries as determined by CTA correctly predicted the particular anterior cerebral artery which preferentially "filled" the aneurysm on DSA (table 2-6)(figures 2-4 and 2-5).

The one patient in this series who had an aneurysm clip in place at the time of CTA had an image with beam-hardening artifact which obscured the aneurysm complex. This patient, however, had another aneurysm which was easily detected by CTA despite

the presence of the clip. In two patients CTA accurately distinguished internal carotid artery-anterior choroidal artery aneurysms from posterior communicating artery aneurysms (figure 2-6).

Discussion

The sensitivity and specificity of CTA for aneurysm detection in our series of patients was 86% and 90%, respectively. This experience is similar to that of others who have examined patients with SAH (7,11,14). Hope et al (7) reported a sensitivity of 90% and specificity of 50% in a series of 80 patients with symptomatic aneurysms, although the number of these with acute SAH was not stated. In a report which examined 22 SAH patients Ogawa et al found CTA had a sensitivity of 77% and specificity of 87% (11), and in a series of 30 SAH patients Vieco et al found CTA had a sensitivity of 97% and specificity of 100% (14). Alberico et al examined 23 SAH patients and reported a sensitivity and specificity of 96% and 100%, respectively, with an interobserver variability of 10% (1).

Six of our CTA examinations were falsely negative, compared to DSA, and two of these were because the aneurysm was located in the posterior fossa. We now have adopted a protocol to routinely include the posterior fossa to ensure a complete examination in every case of acute SAH (120 cc of contrast @ 3 cc/sec, 1.4:1 pitch, and a volume spanning 30 mm above and below the sella floor). The other 4 falsely negative CTA studies were due to aneurysms less than 4 mm in diameter, and this finding, along with our single false positive detection of a tiny middle cerebral artery aneurysm, is consistent with other reports of diminished sensitivity and specificity of CTA detection of

small aneurysms (1,7,11-14).

In our examination of CTA for aneurysm detection we also objectively compared various anatomical characteristics of aneurysms demonstrated by CTA compared to the DSA control studies. Of the 37 aneurysms seen both on CTA and DSA, the accuracy of CTA for aneurysm lobularity and neck size was 95% and 97%, respectively. However two patients harbored aneurysms that DSA suggested were single-lobed, but CTA and subsequently surgery demonstrated that they were multilobed. Our impression was that in certain cases CTA was superior to DSA in determining aneurysm shape and contour. Arterial branches adjacent to the aneurysm neck were reliably detected by CTA, and in particular in no patient in our series was a major branch missed by CTA. Aneurysm size as assessed by CTA correlated well with DSA results, but like DSA CTA only visualizes the part of the aneurysm dome that fills with contrast agent. Previous studies have only subjectively assessed the anatomical definition of aneurysms by CTA (3,6,11,13). Overall, we found the anatomical information provided by CTA to be excellent, and especially the three-dimensional representations provided by the shaded-surface images were considered helpful to surgical planning.

One of the disadvantages of CTA examinations is the inability to determine temporal (time-related) characteristics of artery and aneurysm filling. This feature might be considered important, for example, in determining which anterior cerebral artery preferentially fills an anterior communicating artery aneurysm, and consequently on which side (right or left) a craniotomy is to be made for aneurysm repair. In the case of anterior communicating artery aneurysms we found that anatomical information provided by CTA, including relative precommunicating anterior cerebral artery size and direction

of aneurysm growth, was able to predict the side that the aneurysm preferentially filled on DSA imaging. This aspect of CTA has not been addressed in previous studies.

There are other drawbacks and areas of caution with CTA. The SSD images provide valuable information about the relation of the skull base to the blood vessels, but the quality and usefulness of these images depends on the level of threshold chosen (Hounsfield Unit level for inclusion of contrast filled vessels), which if incorrect may result in loss of information such as the presence and location of small vessels when the threshold is too high, or distortion of aneurysm and neck size if the threshold is too low. We did not find, however, that the density of acute subarachnoid blood (approximately 80 HU) resulted in any difficulty in thresholding a distinction between blood clot surrounding contrast-filled arteries (generally 110-350 HU). MIP images have a particular disadvantage in which they require post scan processing removal of the skull bones in order for adequate visualization of the blood vessels. This task may be quite difficult in removing the skull base while preserving the supraclinoid internal carotid artery and its branches. We have found that personnel less knowledgeable of cerebrovascular anatomy and inexperienced with manual editing techniques are more likely to produce poorer quality MIP images, especially of the intracranial internal carotid artery and its major branches.

We have limited experience with CTA when an intracranial aneurysm clip is present, although the one patient in the series with a clip showed significant beam-hardening artifact which obscured the aneurysm-clip complex. The artifact was confined to immediately surround the clip, thus allowing identification of an aneurysm at a different site. Our more recent experience not reported here is similar. Vieco and

colleagues reported similar results with intracranial aneurysm clips, however they found that more extensive processing was able to demonstrate residual aneurysm necks by superimposing MIP and SSD images (15). We elect to follow the aneurysm-clip complex postoperatively with DSA.

The advantages of CTA compared to DSA include its rapidity, reduced invasiveness and substantially lower cost (6). The disadvantages of CTA include its difficulty in detecting very small and unusually located aneurysms (including those in the cavernous sinus), aneurysm remnants adjacent to an aneurysm clip, as well as the need for an experienced clinician (neuroradiologist or neurosurgeon) to help the CT-technician edit the reformatted images at the workstation.

Because of its difficulty in detecting small aneurysms CTA is not presently recommended for the screening of asymptomatic patients for familial aneurysms. However, in the setting of SAH where the results of the plain CT and CTA are clear, it is possible to forego DSA prior to emergency surgery. In all other cases, DSA should be performed.

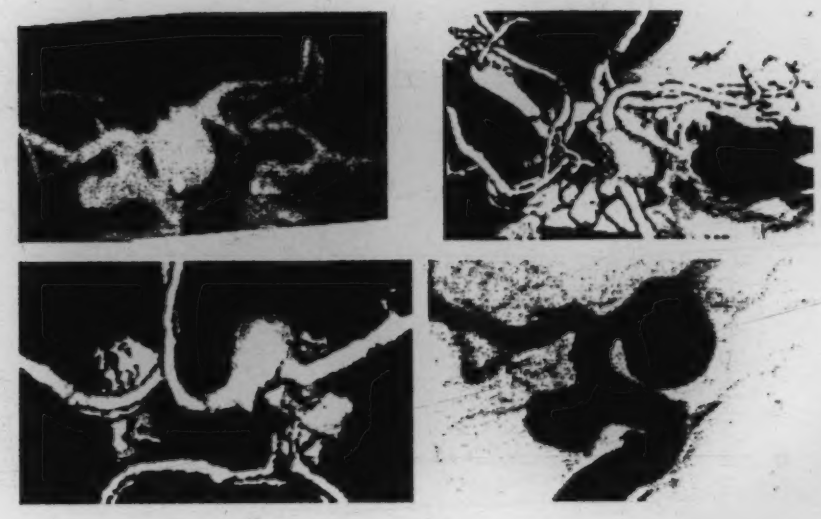

Figure 2-1

Anteroposterior projection of a MIP-CTA from a 51 year old woman with an acute subarachnoid hemorrhage (a), demonstrating right-sided, wide-necked, internal carotid-posterior communicating artery and precommunicating anterior cerebral artery segment (A1) aneurysms, which are also seen on anterosuperior (b) and superior (c) SSD-CTA images. The especially broad neck of the A1 aneurysm, as well as the small aneurysmal excrescence on the superomedial aspect of the A1 segment (arrows) are better appreciated on CTA than on the DSA image (c).

Figure 2-2

Superior SSD-CTA image of the circle of Willis from a 41 year old woman suffering subarachnoid hemorrhage (a) demonstrating a clearly bilobed right middle cerebral artery (M1) bifurcation aneurysm, the shape of which is not as clearly shown on the DSA image (b).

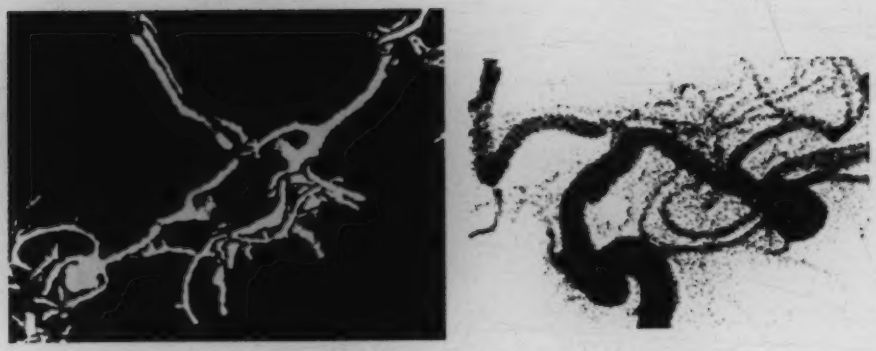

Figure 2-3

Superior SSD-CTA image of the circle of Willis from a 67 year old man with an acute subarachnoid hemorrhage demonstrating a left-sided middle cerebral artery main trunk (M1) termination aneurysm (a); that the termination was a trifurcation was more clearly shown on CTA than on the DSA projections (b).

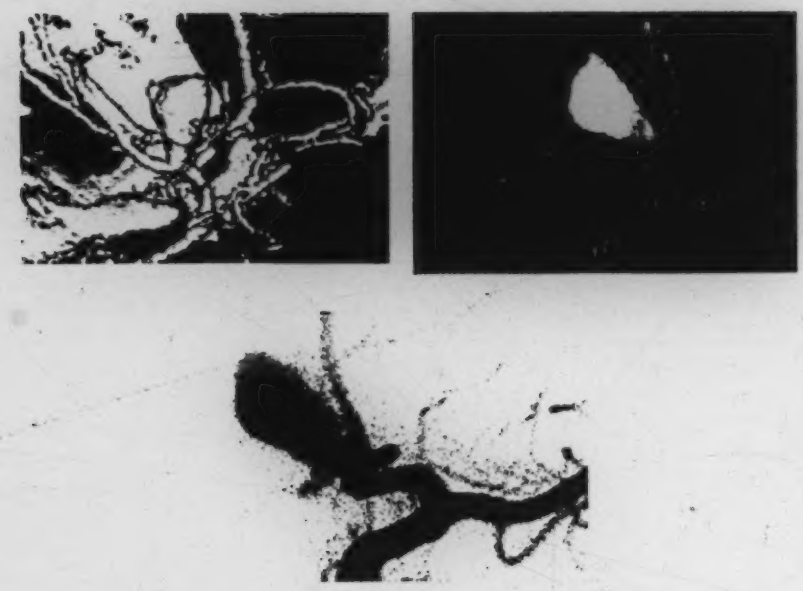

Figure 2-4

Superior SSD image taken from a 44 year old man with an acute subarachnoid hemorrhage, demonstrating a large anterior communicating artery aneurysm arising from the junction of the left A1 segment-anterior communicating artery segment, pointing superiorly and to the right (a), and associated with an atretic right-side A1 artery as shown on the MIP image (b, arrow). DSA imaging confirmed these findings (c).

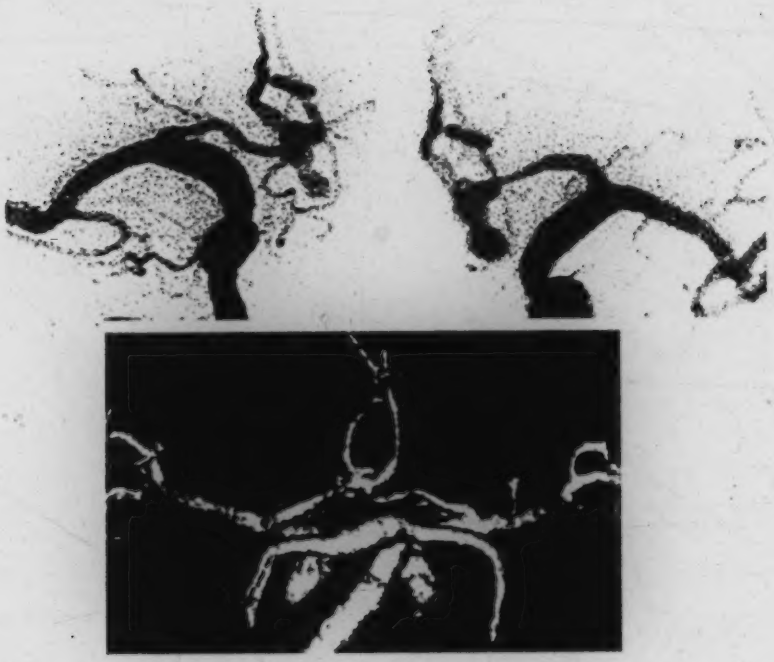

Figure 2-5

Anteroposterior projections of right (a) and left (b) internal carotid DSAs taken from a 64 year old man with acute subarachnoid hemorrhage, demonstrating a centrally located, inferiorly projecting anterior communicating artery aneurysm filling equally from both sides. This information, along with the tapering, mild stenosis of the distal left A1 segment (arrow), was accurately depicted on the superior SSD-CTA image (c).

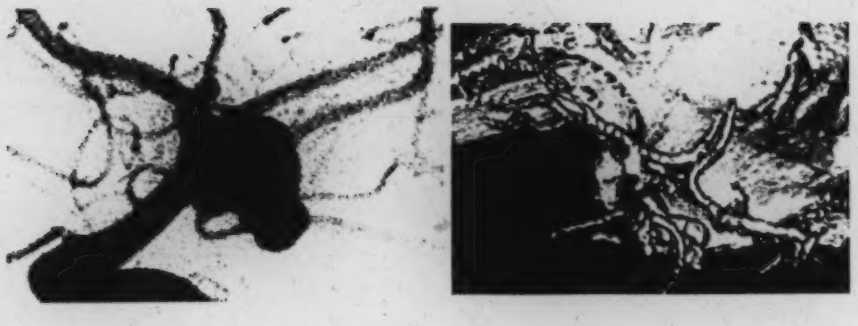

Figure 2-6

Lateral projection of a left carotid DSA taken from a 71 year old man with acute subarachnoid hemorrhage (a), demonstrating a large anterior choroidal-internal carotid artery aneurysm; the aneurysm's broad neck arising distal to the infundibular origin of the posterior communicating artery was clearly seen on the SSD-CTA (arrow, b).

Table 2-1: Aneurysm detection by CTA compared to DSA controls

Aneurysm location[1]	No.	True positive	False negative	False positive
carotid-cav.	2	2	0	0
carotid-ophth.	2	1	1	0
post. comm./ant. choroidal	6	6	0	0
carotid-term.	1	0	1	0
A1	2	2	0	0
ant. comm.	7	7	0	0
A2	1	1	0	0
M1	1	1	0	0
M2	17	16	1	1
basilar	1	1	0	0
PICA	1	0	1	0
AICA	1	0	1	0
PCA	1	0	1	0
TOTAL	43	37	6	1

[1]carotid-cav. = carotid-cavernous, carotid-ophth. = carotid-ophthalmic, post. comm. = posteriorcommunicating, ant. choroidal = anterior choroidal carotid-term = carotid-termination, A1 = pre-communicating segment of anterior cerebral artery, ant. comm. = anterior communicating, A2 = post-communicating segment of anterior cerebral artery, M1 = middle cerebral artery main trunk, M2 = distal middle cerebral artery branch, PICA = posterior inferior cerebellar artery, AICA = anterior inferior cerebellar artery, PCA = posterior cerebral artery

Table 2-2: Aneurysm size

Size (mm)	CTA	DSA
0-5	11	11
6-10	20	21
11-15	5	3
16-20	1	2
21-25	0	0
TOTAL	37	37

Table 2-3: Aneurysm neck size

	DSA		
CTA	**< 4 mm**	**> 4 mm**	**total**
< 4 mm	27	1	28
> 4 mm	0	9	9
total	27	10	37

Table 2-4: Aneurysm lobularity

	DSA		
CTA	**single**	**multiple**	**total**
single	22	0	22
multiple	2	13	15
TOTAL	24	13	37

Table 2-5: Arterial branches at aneurysm origin

No. branches	CTA	DSA
0	5	4
1	10	10
2	19	20
3	3	3
TOTAL	37	37

Table 2-6: Determination of the direction of anterior communicating aneurysm filling

Patient	larger A1[1] (by CTA)	neck location on ant. comm. artery[2]	direction of aneurysm projection	aneurysm filling side by DSA
1	R=L	R=L	ant.	R=L
2	R	R	left, ant.	R
3	R	R	left, ant.	R
4	R	R=L	ant.	R
5	L	L	right	L
6	L	L	right	L
7	R	R=L	inf.	R

[1]A1 = pre-communicating segment of anterior cerebral artery

[2]ant. comm. = anterior communicating artery

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CT Angiography versus Digital Subtraction Angiography for the Diagnosis and Early Treatment of Ruptured Intracranial Aneurysms[1]

[1] A version of this chapter has been published. Anderson. *Neurosurgery* in press.

Introduction

Computed tomographic angiography (CTA) is a rapid, minimally invasive, and convenient method to detect cerebral aneurysms following a plain CT scan demonstrating subarachnoid hemorrhage (SAH). In many cases CTA will inform the clinician immediately if the patient is harbouring a ruptured aneurysm, and appropriate planning and treatment can then begin. In some patients the quality of the CTA images is such that the added value of obtaining a digital subtraction angiogram (DSA) before surgical aneurysm repair, with its attendant risks, delay, and cost, is called into question.

A number of investigators (1-7,9,11-12, 14-16,18-21,23-25,27) have reported their initial experience with CTA in the detection of cerebral aneurysms following SAH, generally indicating its utility and anatomical accuracy. In this study we set out to answer a purely clinical question: how often can urgent aneurysm surgery be performed safely based entirely on preoperative CTA?

Patients and Methods

The University of Alberta Hospital possesses the only neurosurgical service in Northern Alberta and provides care for all patients suffering aneurysmal SAH. In a prospective study, 173 consecutive patients treated in our hospital for recognized SAH were assessed in this study. Patients with severe hemorrhages inconsistent with survival were not examined with angiography of any type following plain CT scanning, and were therefore not included in this study. All other otherwise unselected patients were examined. Since CTA was considered a priority to be a proven diagnostic test for intracranial aneurysms, and the treating surgeons were prepared to operate on the basis of CTA results, consent for patient involvement in this paradigm was not obtained.

Following plain CT scanning diagnostic for SAH, CTA was carried out. The CTA examinations, as well as the post-scan image processing, were performed by CT technologists. The CTA and plain CT of the head were reviewed by the neurosurgeon caring for the patient (any one of three surgeons), often assisted by a neuroradiologist, and based upon the information available, a decision was made to obtain a DSA, or proceed directly to surgery for aneurysm repair.

CTA was performed using a General Electric Spiral CTi scanner (General Electric, Milwaukee, WI), and images were processed with the General Electric Advantage Windows 3-D workstation. An initial test injection and scan was performed to determine the circulation time to peak enhancement of the cavernous internal carotid artery. Optiray 320 (Mallinkrodt Medical, Pointe Claire, Quebec, Canada) was injected via an antecubital vein at 3cc/sec for a total of 20cc, and 25 scans are obtained at the level of the midsella turcica after a 10 second delay. The resultant time to peak intensity, minus 2 seconds, was used as the scan delay for the CTA. The formal CTA consisted of 120cc of contrast also injected at a rate of 3cc/sec, with a scan delay as determined in the test dose. The scan volume included 30mm above and below the sella turcica. A collimation width of 1mm, 1:4 pitch, 15cm field of view, 120kV, and 280-300mA were used. The axial source images were then reconstructed to 0.5mm overlapping sections to increase resolution. The reconstructed images were then processed on the workstation into shaded surface display (SSD) and maximum intensity projection (MIP) images. Images were the pictured at 15 degree intervals covering 180 degrees in two planes.

Digital subtraction angiography was performed using the Seldinger technique with femoral puncture and selective 4-vessel cerebral catheterization, obtaining anteroposterior, lateral, and oblique images.

Statistical testing was performed using the Mantel-Haenszel Chi Squared test.

Results

A total of 173 patients underwent angiography to detect acutely ruptured aneurysms during the study period. There were 103 female and 70 male patients with an age distribution of 30-88 (Table 3-1). Of the patients that underwent surgical repair, 70% were of a Hunt-Hess grade (13) of II-III. In 24 patients (Hunt-Hess grade I-II) both CTA and repeated DSAs were negative for aneurysms or any other source of bleeding. Twelve patients in the first six months of the study underwent DSA only prior to surgery, as a technologist able to perform CTA was not available. A total of 9 patients underwent CTAs diagnostic for ruptured aneurysms, but due to poor neurological condition (Hunt-Hess grade IV-V) were not considered for either DSA or aneurysm repair at any point.

All 9 patients subsequently died. Two patients were found to have an arteriovenous malformation on the initial CTA and confirmed on the subsequent DSA.

Of the remaining 126 patients who underwent aneurysm clipping, 65 (52%) underwent DSA following CTA and prior to surgery. The decision to proceed to DSA was influenced by aneurysm location, with aneurysms originating adjacent to the skull base (where CTA cannot reliably distinguish vessel from bone) more often required DSA for full clarification. For example, 66% ($0.025 > P > 0.01$, as compared to all aneurysms) of middle cerebral artery (MCA) aneurysms (fig. 3-1) underwent surgery with just CTA imaging, while only 38% ($0.25 > P > 0.10$) of posterior communicating artery aneurysms proceeded to repair following CTA alone (fig. 3-3) (Table 3-2). Anterior communicating artery aneurysms (fig. 3-2) were more equally divided into the two groups with 53% ($P > 0.25$) proceeding to surgery with CTA alone. Overall, testing for association between aneurysm site and the requirement of DSA was significant ($0.025 > P > 0.01$). In 12 of the 18 patients with posterior communicating artery aneurysms who underwent both CTA and DSA prior to surgery, DSA aided in clarifying the neck and dome morphology. In 9 of the 19 patients with anterior communicating artery aneurysms and 4 of the 12 patients with middle cerebral artery aneurysms who underwent CTA and DSA prior to surgery, DSA aided in clarifying aneurysm morphology as well as the number and location of adjacent arterial branches.

For those patients who underwent both CTA and DSA before surgery, the sensitivity and specificity for aneurysm detection by CTA, as compared to the preoperative DSA, was 84% and 100%, respectively (Table 3-5). Fifteen aneurysms, including 4 in one unusual patient and 3 in two others, were missed by CTA, and all were less than 4mm in size (Table 3-3). None of these small aneurysms ended up being repaired at the time of surgery for the ruptured aneurysm.

In 61 patients who underwent preoperative CTA (48% of the total), surgery was based just on the results of CTA. The sensitivity and specificity for aneurysm detection in this group, as compared to postoperative DSA was 90% and 100%, respectively (Table 3-5). Eight aneurysms were not detected on the preoperative CTA, and again all were less than 4mm in size (Table 3-4). In one patient the undetected aneurysm would have resulted in different surgical management had it been detected by CTA. This patient first

underwent acute repair of a small posterior inferior cerebellar artery (PICA) aneurysm, clearly seen on CTA (fig. 3-4) in the setting of diffuse SAH. However at surgery that aneurysm did not have the appearance of a ruptured aneurysm, prompting an immediate postoperative DSA which revealed a smaller (3mm) posterior communicating artery aneurysm more clearly responsible for the SAH. This aneurysm was repaired with a second operation. In the 43 other cases there were no instances where the performance of the surgery was considered misdirected by the absence of DSA information.

There were a total of 24 aneurysms (16 in the CTA and DSA preop. group and 8 in the CTA only preop. group) missed by CTA. All of these aneurysms were in patients with multiple aneurysms. In this series 32 of the 147 (22%) patients with a documented aneurysm had multiple aneurysms. Of these 32 patients CTA missed at least one aneurysm in 15 patients (Table 3-6).

Discussion

Using DSA as the gold standard, numerous reports have demonstrated the high sensitivity and specificity of CTA in detecting cerebral aneurysms (1-5,7-12,14-15,18-25,27). However, in these studies CTA was undertaken to compliment, rather than replace DSA in radiographic aneurysm definition.

The purpose of this study was to examine a practical clinical issue, which is the feasibility of performing aneurysm surgery based on the results of CTA. Prior to this report there has been only one other series that examined the clinical implications of surgical planning based on preoperative CTA (27). Zouaoui et al reported that 40 patients out of 120 (33%) underwent aneurysm clipping based just on CTA. They found no discrepancies between preoperative CTA and postoperative DSA.

Velthuis et al (24) recently indicated, from a retrospective examination of patients who underwent both CTA and DSA, 74% of 100 patients could have undergone aneurysm surgery based on CTA alone. However in that study all patients underwent CTA and DSA preoperatively and no patient had surgery based on CTA alone. Postoperative examination of the CTA's was performed by neurosurgeons and a decision was made whether or not CTA information was sufficient to have performed surgery without DSA.

In this prospective study we wanted to objectively determine if we could safely perform surgery for acutely ruptured aneurysms based solely on CTA. The patients in our series underwent CTA and then a decision was made to proceed to surgery or to DSA. We found that in a total of 126 patients who underwent preoperative CTA the information provided by CTA was considered sufficient to undertake an operation in 48% of patients. CTA demonstrated with good specificity ruptured aneurysms larger than 4 mm. in diameter in common aneurysm locations. The anatomical definition provided by CTA in terms of aneurysm size, shape, neck characteristics, and orientation, as well as adjacent arterial branches is generally very good (3). The combination of a good quality CTA image and a plain CT scan demonstrating a pattern of hemorrhage consistent with the identified aneurysm enabled safe surgery on the basis of CTA results alone.

A total of 24 aneurysms (in126 patients) were missed by CTA and all of these were in patients with multiple aneurysms. The ruptured aneurysm was detected by CTA in all cases except one (mentioned in the results). In 47% (15/32) of the multiple aneurysm patients in this series at least one aneurysm was missed by CTA. This might be partly explained by a processing and interpreting bias after the obviously ruptured aneurysm was found, since in a number of cases retrospective analysis of the CTA did reveal the additional aneurysm(s). Early in this study, inexperienced technicians performing CTA's as well as a relative unfamiliarity in reading the CTA's by treating neurosurgeons and neuroradiologists at our institution also influenced aneurysm detection by CTA.

We found middle cerebral artery aneurysms more commonly underwent surgery based on CTA alone, whereas posterior communicating artery tended to undergo both CTA and DSA prior to surgery. Anterior communicating artery aneurysms were more evenly split. The difficult task of separating posterior communicating artery aneurysms from the skull base on CTA may explain a tendency for these aneurysms to proceed to DSA for further clarification. The relative increased complexity of adjacent arterial branches of anterior communicating artery aneurysms, compared to middle cerebral artery aneurysms, may explain an increased tendency for these aneurysms to proceed to DSA preoperatively.

The principal problem with CTA is its difficulty in detecting small aneurysms less than 4mm in size. A number of such aneurysms were missed in the group of patients operated on with CTA results alone, although they were mainly incidental discoveries on postoperative DSA, not requiring immediate, or in most cases, any treatment (8 of the 24 missed aneurysms were cavernous ICA aneurysms not requiring any treatment). The possibility exists, nevertheless, that if such an aneurysm was unrecognized on preoperative imaging, an opportunity to repair it during surgery for a nearby ruptured aneurysm would be missed. We did treat one unusual patient (fig. 3-4), who first underwent surgery for an unruptured PICA aneurysm, on the basis of a CTA which failed to detect a smaller ruptured p-comm. aneurysm. However, since the original pattern of bleeding was diffuse, and the ruptured aneurysm was very small (3mm), and smaller than the aneurysm repaired first, it is probable that even if both aneurysms had been detected preoperatively on DSA the wrong one would still have been repaired first.

Recently the International Study of Unruptured Intracranial Aneurysms (28) reported the rupture rate for aneurysms < 10 mm to be roughly 0.5%/yr. for patients with a prior history of SAH. This low rupture rate calls into question the advisability of at least an extensive additional dissection that might be required to repair a small aneurysm distant to the ruptured aneurysm. The preoperative detection of all small, unruptured aneurysms may therefore, not always be critical.

We have found that the acquisition of CTA, which is simple, fast, and safe, almost always assists aneurysm treatment and surgery. We value the convenience and benefit of avoiding the delays in surgery and risk that preoperative DSA imposes. We remain cognizant, however, that when surgery proceeds on the basis of CTA alone the risk of that approach is that a small, unruptured, and nearby aneurysm might be missed, and therefore not specifically identified and repaired at the time of surgery.

Balancing these two factors, it is our continuing practice to operate on the basis of CTA alone in selected patients. In all such patients we believe that postoperative DSA is mandatory. It seems likely that continued refinement of CTA and greater experience with its use will increase its sensitivity for small aneurysms.

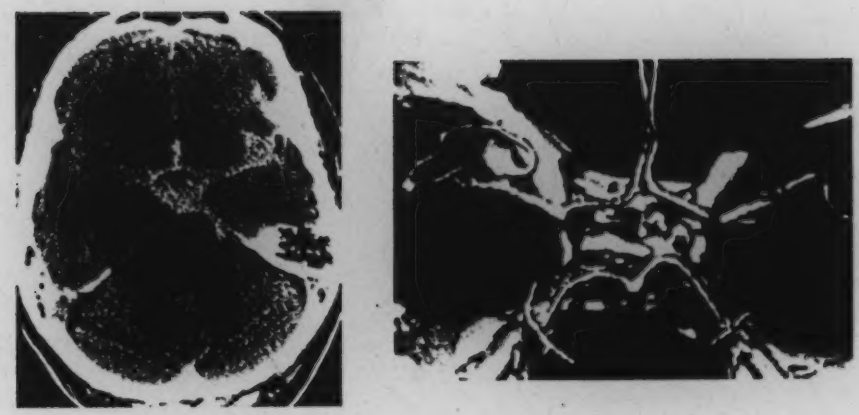

Figure 3-1

55 year old patient with acute subarachnoid hemorrhage demonstrated on plain CT (a). Shaded surface display CTA (b) demonstrates a middle cerebral artery aneurysm (arrow). The patient underwent surgical clipping without any further investigation.

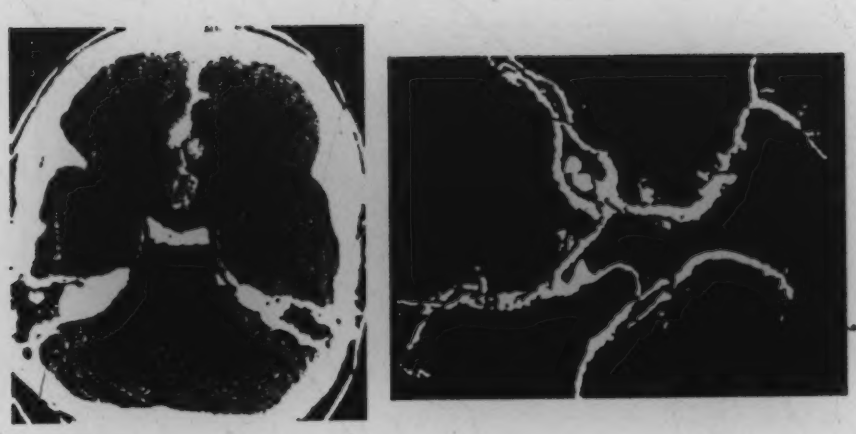

Figure 3-2

Plain CT (a) demonstrating an interhemispheric subarachnoid hemorrhage. An anterior communicating artery aneurysm (arrow) was clearly defined by CTA. No further preoperative imaging was performed.

Figure 3-3

48 year old patient with an acute intraventricular hemorrhage (arrow) on plain CT (a). Preoperative imaging consisted of only CTA (b) clearly showing a posterior communicating artery aneurysm (arrow).

Figure 3-4

Grade III subarachnoid hemorrhage patient with diffuse SAH and fourth ventricular clot (arrow) shown on plain CT (a). Maximum intensity projection CTA (b) revealed a posterior inferior cerebellar artery aneurysm (arrow). This aneurysm was surgically repaired, but was found to be intact, and a digital subtraction angiogram (c) performed the next day revealed a posterior communicating artery aneurysm (arrow) responsible for the hemorrhage. The patient underwent a second operation to clip the second aneurysm.

Table 3-1 Patient Characteristics By Preoperative Angiographic Modality

Gender	CTA only	CTA & DSA	DSA only
male	23	40	7
female	47	51	5
Grade[1]			
I	15	24	4
II	21	31	7
III	19	29	1
IV	8	5	0
V	7	2	0
Age (yr.)	36-88	30-76	42-70

[1] Hunt-Hess SAH grade

Table 3-2 Frequency of Surgery with CTA only or CTA and DSA Preoperatively by Aneurysm Site

Location	CTA only (%)	CTA & DSA (%)
MCA	23 (66)	12 (34)
A-comm	21 (53)	19 (47)
P-comm	11 (38)	18 (62)
Basilar	1 (33)	2 (67)
PICA	1 (25)	3 (75)
Pericallosal	1 (33)	2 (67)
Ophthalmic	1 (25)	3 (75)
ICA	2 (25)	6 (75)

MCA= middle cerebral artery, A-comm= anterior communicating artery, P-comm= posterior communicating artery, PICA= posterior inferior cerebellar artery, ICA= internal carotid artery

Table 3-3 Aneurysms Undetected by CTA in Patients with Preoperative CTA & DSA

Patient	Location	Size mm
1	Sup. Hypophyseal	2
2	A-comm	3
	MCA	3
	Pericallosal	2
3	ant. Choroidal	3
	cavernous ICA	2
	cavernous ICA	3
4	A-comm	3
	MCA	3
	P-comm	2
	Ophthalmic	4
5	cavernous ICA	2
6	cavernous ICA	2
7	cavernous ICA	1
8	sup. Cerebellar	2
9	cavernous ICA	2

Sup. Hypophyseal= superior hypophyseal artery, A-comm= anterior communicating artery, MCA= middle cerebral artery, ant. Choroidal= anterior choroidal artery, ICA= internal carotid artery, P-comm= posterior communicating artery, sup. Cerebellar= superior cerebellar artery

Table 3-4 Aneurysms Undetected by CTA in Patients with Preoperative CTA only

Patient	Location	Size mm
1	ICA terminus	2
2	P-comm	2
3	Pericallosal	4
4	P-comm	3
5	ICA cavernous	2
6	ICA cavernous	3
	P-comm	2
	Ophthalmic	2

ICA= internal carotid artery, P-comm= posterior communicating artery,

Table 3-5 CTA Aneurysm Detection as Compared to DSA

	Pre-op CTA	Pre-op CTA & DSA
Sensitivity	90	84
Specificity	100	100

Table 3-6 Number of Patients and CTA Aneurysm Detection in Patients with Multiple Aneurysms

	No. pts with multiple aneurysms	CTA undetected aneurysms
CTA & DSA	19/65 (29%)	9/19 (47%)
CTA only	13/61 (21%)	6/13 (46%)
DSA only	0/12 (0%)	na
nonsurgical CTA only	0/9 (0%)	na
Total	32/147 (22%)	15/32 (47%)

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CT Angiography for the Detection of Cerebral Vasospasm In the Setting of Acute Subarachnoid Hemorrhage

Introduction

Vasospasm is on of the leading causes of morbidity and mortality in patients who survive an initial subarachnoid hemorrhage (SAH)(18). Up to 50% of SAH patients may develop cerebral vasospasm to some degree (1). Vasospasm typically occurs 7-10 days post bleed and its prompt diagnosis is required in order to initiate appropriate therapy to avoid ischemic insults. The current gold standard for detecting vasospasm is digital subtraction angiography (DSA). DSA provides an accurate depiction of the intracranial vessels and the aneurysm-clip complex. There is a significant risk with DSA, however, a total complication rate of ~5% and permanent stroke rate of ~.5-1% has been reported (5, 6, 11, 16, 17). CT angiography (CTA) does not have the neurological risks of DSA, is cheaper, quicker, and has been shown to depict the intracranial vasculature well in the setting of SAH (2, 3, 4, 7, 9, 19). The purpose of this study, thus was to compare CTA with DSA in the ability to accurately detect cerebral vasospasm in patients suffering SAH.

Methods

In this prospective study, patients presenting with SAH, diagnosed on plain CT, then underwent CT angiography. Between day 5-10 post bleed patients then underwent CTA and DSA, within 24 hrs. of each other. The initial and delayed CTA exams were performed in the same manner. An initial test bolus (20cc) of contrast (Optiray 320, Mallinkrodt Medical, Pointe Claire, Quebec) was infused (3cc/sec.) via an antecubital 20 gauge i.v. catheter. After a 10 sec. delay 25 nonhelical axial cuts were taken every 1 sec. at the level of the sella turcica. A time to maximal intensity (HU) graph was made on the scanner and a scan delay time for the CTA was taken at the time of maximal luminal enhancement (internal carotid artery). The formal CTA consisted of 120cc contrast (Optiray 320) infused at 3cc/sec. via the antecubital i.v. Helical scanning the commenced after the appropriate scan delay as calculated in the test infusion. Using a GE CTi scanner (GE, Milwaukee, Wisconsin), 1mm. helical scans were performed from the craniocervical junction to 30mm. above the floor of the sella. The pitch was 1.4 with 280-320mA, 200kHz. The 1mm. source axial images were then reconstructed to 0.5mm. axial

images. The reconstructed images were then transferred to a computer workstation (GE Advantage Windows) for 3-D reconstruction. Maximum intensity projection (MIP) images were produced by initial bone removal by a thresholding technique then manual editing was performed to remove any remaining bone of the skull base. All MIP reconstructions were performed by the same experienced investigator (GBA). The MIP images were pictured every 30 degrees while rotating through 180 degrees in 2 planes.

The DSA exams were performed using the transfemoral Seldinger technique with anteroposterior, lateral, and lateral oblique views imaged.

The CTA and DSA exams were reviewed by separate investigators. The initial and delayed CTA exams were compared for presence of spasm and these results were then compared to the corresponding DSA. Six arterial locations were examined: suprasellar internal carotid artery (ICA); M1 and M2 segments of the middle cerebral arteries; A1 and A2 segments of the anterior cerebral arteries; and the basilar artery. Using calipers and a finely calibrated ruler the degree of vasospasm was categorized as follows: none; mild (<30% luminal narrowing); moderate (30-50% luminal narrowing); and severe (>50% luminal narrowing).

The CTA and DSA exams were compared using Spearman correlation coefficient, sensitivity, specificity, accuracy, and predictive values. Statistical significance was calculated using Fisher's exact test.

Results

A total of 17 patients were studied. The overall agreement between CTA and DSA over all locations and degrees of vasospasm was 86% (table 4-1) with a correlation coefficient of 0.757 ($p<0.001$). The best agreement and correlation between CTA and DSA by location was for the more proximal sites: ICA, M1 (fig. 4-2), A1 (fig. 4-1), and basilar (fig. 4-3) arteries (table 4-1). The distal arterial locations (A2, M2) had a poorer overall degree of correlation. At all locations, agreement between CTA and DSA was greater for no or severe spasm with detection of mild or moderate spasm by CTA as poorer (table 4-1).

CTA tended to overestimate the degree of spasm at the proximal locations and equally over and underestimated the degree of spasm at the distal sites. In general, most

discrepancies between CTA and DSA were in the mild and moderate degree of spasm categories.

Table 4-2 displays various statistical parameters comparing CTA with DSA over all locations for each degree of spasm. CTA is highly sensitive and accurate in detecting no or severe spasm, however, for mild or moderate spasm CTA is much less sensitive, but remains quite specific. If we examine the data for no or mild spasm together CTA remains highly sensitive and accurate, with moderate specificity. For moderate and severe spasm together, CTA was moderately sensitive, but very specific and accurate.

On the initial examination of the data (table 4-1) CTA was found to correlate with DSA to a greater degree for the proximal arterial locations (correlation coefficient 0.921 vs. 0.348 for distal location, $p<0.001$). Tables 4-4 show various statistics for proximal versus distal sites. Comparing table 4-3 with table 4-2 in general, CTA is more sensitive and accurate for proximal, as compared to distal locations. CTA is highly sensitive, specific, and accurate for no or severe spasm, however, sensitivity and accuracy are poorer for detection of mild and moderate degrees of spasm (table 4-3). For no or mild spasm together or moderate or severe spasm together, we see CTA remains highly sensitive, specific, and accurate (table 4-3).

Examining the data for distal arteries (A2, M2) we found generally poorer results than for proximal location (table 4-4). Detection of severe spasm by CTA was still perfect, but for no spasm CTA was moderately sensitive and poorly specific. The sensitivity for CTA in detecting mild and moderate spasm in distal arteries was very poor. In detecting no or mild spasm CTA was highly sensitive and accurate, however poorly specific. The converse was true for detection of moderate or severe vasospasm (table 4-4).

In this series 9% (15/172) arteries were not assessable on the follow up CTA (table 4-1). One third of these were at the A1 segment and the ICA and M2 segments roughly had a third each. In each of these cases where the artery was not adequately visualized for measurement, it was due to aneurysm clip artifact. At our institution titanium clips are not routinely used therefore considerable clip artifact occurs on the CTA. This artifact typically involves 4-5mm. around the clip making assessment of the

aneurysm remnant-clip complex impossible to assess as well as any arteries in this artifact range impossible to examine.

Discussion

Cerebral vasospasm if undetected and and untreated can cause significant morbidity in SAH patients. Most institutions routinely perform DSA 7-10 days post SAH in order to detect vasospasm. To date DSA has been the mainstay for spasm detection, however, transcranial doppler is a noninvasive method widely employed. This tool is advocated as an initial screening tool since its accuracy is less than ideal (15). CTA is a minimally invasive technique previously demonstrated to accurately depict the intracranial vasculature in the setting of SAH (7-9, 19). To date there has been little reported about the application of CTA in detecting vasospasm post SAH. An initial study involved 2 patients reporting similar depictions of spasm between CTA and DSA, however no objective measurements were made (10).

Since that initial study there has been a few reports of CTA accurately depicting spasm in studies for aneurysm detection post SAH. Zaououi et al (19), in their series of 120 SAH patients found vasospasm on CTA in 5 patients. Similarly, Velthuis et al (14) reported 3 cases of vasospasm on CTA in their series of 80 patients. One study (13) performed CTA on 11 patients postoperatively and found 3 cases of vasospasm. None of these studies initially set out to examine the utility of CTA in detecting vasospasm, and there were formal objective measurements.

A recent study examining the detection of vasospasm by CTA involved 12 patients (12). They compared CTA to DSA in 7 patients found to have spasm on the initial CTA. Of these 7 patients 5 had severe (>75% luminal reduction) and 2 had moderate spasm (50-75% reduction). All 7 of these patients would be classified as severe spasm by the classification scheme used in this series and thus their detection rate by CTA is the same as ours, 100%. They did not objectively assess for normal or less than 50% spasm as we have done in this series.

We have found CTA to be an ideally suited modality for investigating SAH patients for vasospasm. Typically these patients will require a plain CT of the head at which point a CTA can be performed without the added time, expense, and expertise required for DSA. In order for CTA to be able to replace DSA in this capacity its

accuracy needs to be substantiated, and this is what we tried to accomplish in this study. We, like Takagi et al (12), found CTA to be perfect in detecting severe spasm (>50% luminal reduction). CTA was also found to be highly sensitive and accurate for detecting no spasm. Vasospasm was best detected in proximal arterial locations (ICA, A1, M1, and basilar arteries) as well as for no or severe spasm. Mild or moderate spasm (1-50%) was less well detected, especially in distal locations (A2, M2).

We had several cases in which an artery could not be assessed due to aneurysm clip artifact. Thus the presence or absence of spasm was unknown on the CTA. The aneurysm-clip complex was also not assessable due to the clip artifact. These are important disadvantages of CTA as the presence of an aneurysm remnant may require further treatment. The use of titanium clips greatly reduces the amount of artifact (13), but cost presently limits their routine use.

In summary, we have found CTA to be highly accurate in detecting no or severe vasospasm in proximal arterial location, as compared to DSA. Aneurysm clip artifact remains a problem and thus the importance of the knowledge of the periclip-aneurysm complex must be considered if CTA is to replace DSA in the routine postoperative care of SAH patients.

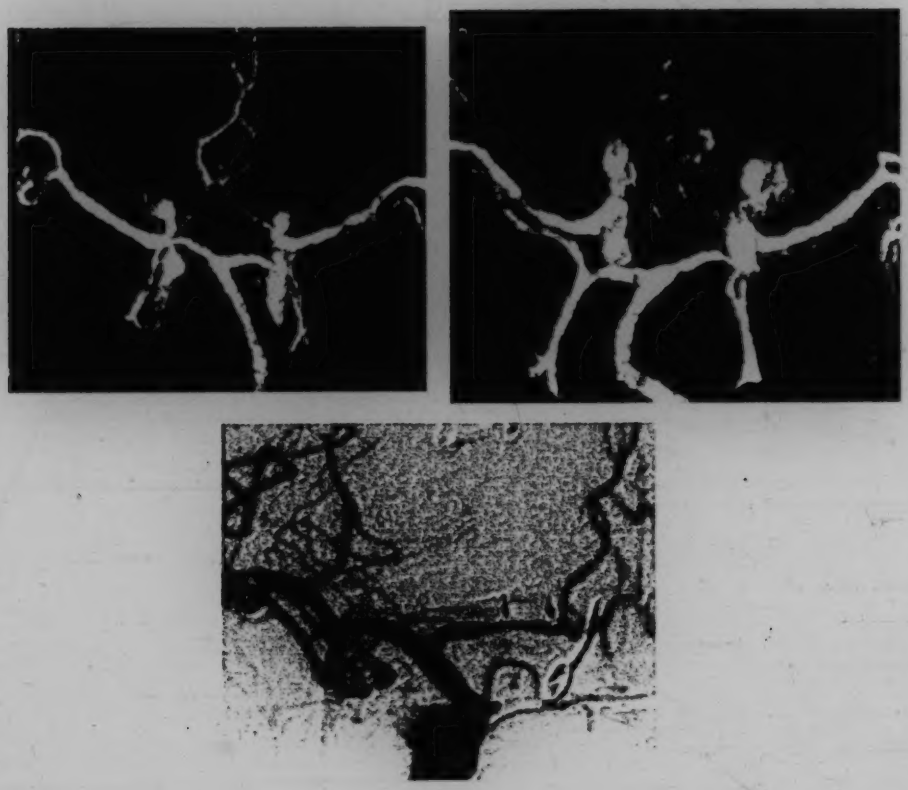

Figure 4-1
Patient sustaining SAH from anterior communicating artery aneurysm rupture with preop. CTA (a). Postop. CTA (b) and DSA (c) revealing A1 spasm (arrows).

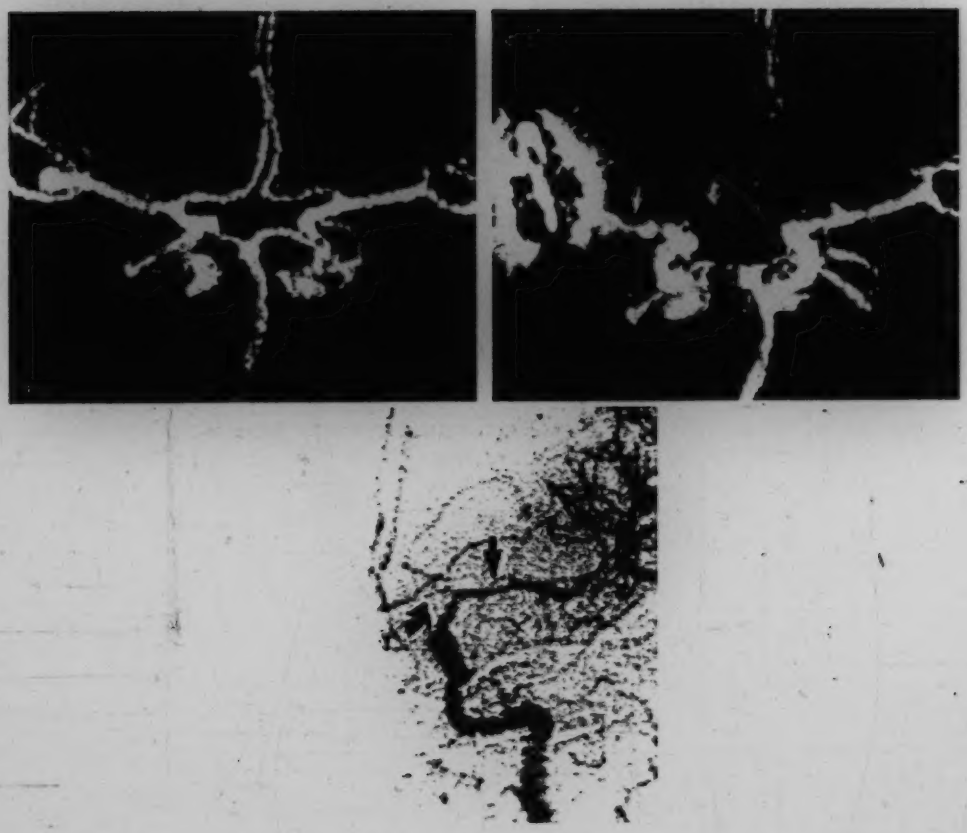

Figure 4-2
Preop. CTA (a) of a patient sustaining SAH from middle cerebral artery aneurysm rupture. Postop. CTA (b) and DSA (c) showing A1 and M1 vasospasm (arrows).

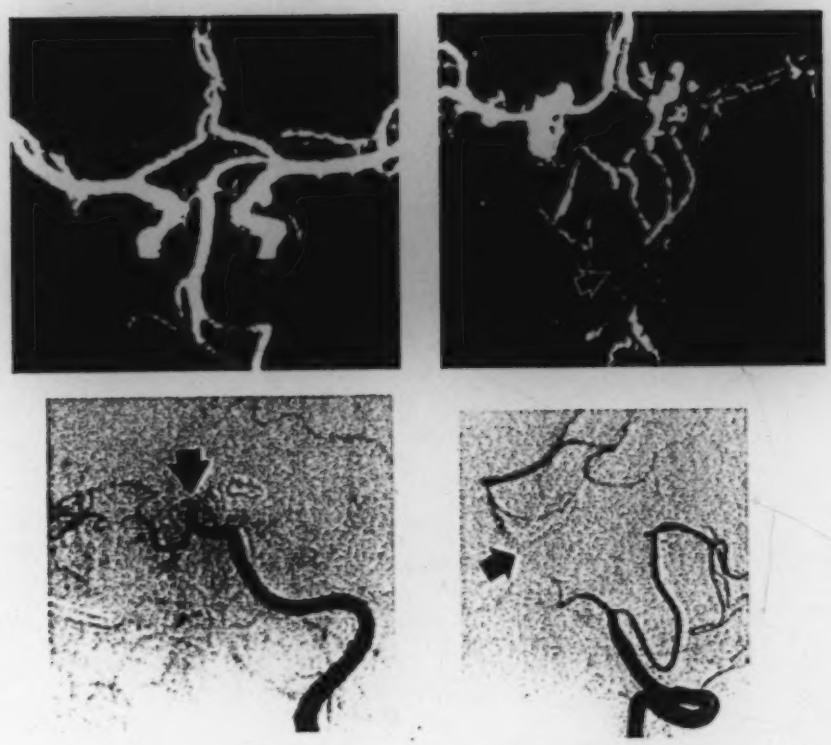

Figure 4-3
Posterior communicating artery aneurysm causing SAH as seen on preoperative CTA (a). Postop. CTA (b) reveals severe basilar artery spasm and carotid artery occlusion (arrows). Basilar artery spasm confirmed on DSA (c) and carotid occlusion seen on DSA (d).

Table 4-1 Agreement Between CTA and DSA by Location and Spasm Degree

Location	Degree of spasm				total	NA	r*
	none	mild	moderate	severe			
ICA	100% (24/24)	80% (4/5)	0 (0/0)	100% (1/1)	97% (29/30)	4	0.998
M1	96% (22/23)	33% (2/6)	100% (2/2)	100% (1/1)	84% (27/32)	2	0.88
M2	88% (23/26)	0 (0/3)	0 (0/1)	0 (0/0)	77% (23/30)	4	0.152
A1	88% (14/16)	100% (6/6)	80% (4/5)	100% (2/2)	90% (26/29)	5	0.92
A2	85% (22/26)	33% (1/3)	33% (1/3)	100% (2/2)	76% (26/34)	0	0.446
Basilar	100% (16/16)	0 (0/0)	0 (0/0)	100% (1/1)	100% (17/17)	0	1
total	92% (121/131)	57% (13/23)	64% (7/11)	100% (7/7)	86% (148/172)	15	0.757

NA=not assessable, r= Spearman correlation coefficient

ICA=internal carotid artery, M1=first segment middle cerebral artery, M2=second segment middle cerebral artery, A1=first segment anterior cerebral artery, A2=second segment anterior cerebral artery

Table 4-2 Statistics by Degree of Spasm for all Locations

Spasm	sens.	spec	PPV	NPV	acc.	P value
none	92%	80%	94%	77%	90%	<.001
mild	57%	93%	54%	93%	88%	<.001
none/mild	**97%**	**78%**	**97%**	**74%**	**95%**	**<.001**
mod.	64%	97%	58%	98%	95%	<.001
severe	100%	100%	100%	100%	100%	<.001
mod/sev.	**78%**	**97%**	**74%**	**97%**	**95%**	**<.001**

Sens.=sensitivity, spec.=specificity, PPV=positive predictive value, NPV=negative predictive value, acc.=accuracy

Table 4-3 Statistics by Degree of Spasm for Proximal Locations

Spasm	sens.	spec	PPV	NPV	acc.	P value
none	95%	96%	98%	90%	96%	<.001
mild	71%	95%	75%	93%	90%	<.001
none/mild	**95%**	**91%**	**99%**	**71%**	**95%**	**<.001**
mod.	86%	95%	60%	99%	95%	<.001
severe	100%	100%	100%	100%	100%	<.001
mod/sev.	**91%**	**95%**	**71%**	**99%**	**95%**	**<.001**

Sens.=sensitivity, spec.=specificity, PPV=positive predictive value, NPV=negative predictive value, acc.=accuracy

Table 4-4 Statistics by Degree of Vasospasm for Distal locations

Spasm	sens.	spec	PPV	NPV	acc.	P value
none	87%	42%	87%	42%	78%	0.039
mild	17%	88%	13%	91%	81%	0.567
none/mild	**98%**	**50%**	**95%**	**75%**	**94%**	**0.002**
mod.	25%	98%	50%	95%	94%	0.122
severe	100%	100%	100%	100%	100%	<.001
mod/sev.	**50%**	**98%**	**75%**	**95%**	**94%**	**0.002**

Sens.=sensitivity, spec.=specificity, PPV=positive predictive value, NPV=negative predictive value, acc.=accuracy

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CT Angiography for the Detection and Characterization of Carotid Artery Bifurcation Disease

Introduction

CT angiography (CTA) is a relatively new method of imaging the cerebral vessels. It has been shown to have a role in detecting ruptured cerebral aneurysms (1-5). More recently CTA has been used to study the carotid artery bifurcation (6-22). The current gold standard for detecting carotid stenosis is digital subtraction angiography (DSA), although DSA is not an entirely benign investigation with total complication rates near ~5% in some reports, and causing permanent strokes in ~0.5% of patients studied (23-26). There is a need for a less invasive investigation for carotid artery disease. One technique is doppler ultrasound which poses little risk to the patient. Ultrasound's application in carotid artery bifurcation disease has been well studied and reported to have a relatively high sensitivity compared to DSA (27-35). The main problem with ultrasound is it's high inter-observer and inter-machine variability (19, 31). Recent reports have suggested that CTA has a high accuracy as compared to DSA (14, 17, 20, 36).

There have been several recent clinical trials reporting the effectiveness of carotid endarterectomy over medical therapy in reducing stroke risk (37-40). The results of these studies apply for patients with specific angiographically determined degrees of stenosis. In symptomatic patients carotid endarterectomy was first shown clearly superior to medical therapy for >69% (39) stenosis. In asymptomatic patients surgery was superior to medical therapy for >60% stenosis (41). More recently some surgical benefit was demonstrate for selected patients with 50-69% stenosis (40). The NASCET (North American Symptomatic Carotid Endarterectomy Trial) data has revealed the number of patients needed to be treated with surgery to prevent any ipsilateral stroke to be 8 vs. 20 at 2 years for 50-69% and 70-99% stenosis, respectively (40). At five years this becomes 8 vs. 15 patients for 50-69% and 70-99%, respectively. It has also been shown that plaque irregularity and ulceration has an increase stroke rate with medical therapy (42), therefore the precise degree of stenosis and plaque morphology have important management implications. We wanted to see how close CTA can depict the degree of carotid stenosis compared to DSA.

Methods

Forty patients (80 arteries) were studied prospectively. All patients were symptomatic with either transient or permanent hemispheric or ocular symptoms or signs. There were 24 male (age 44-83) and 16 female (age 52-78). All patients underwent initial color coded doppler ultrasound with degree of stenosis calculated based on peak flow velocities. The ultrasound examinations were performed at several different laboratories, and although these ultrasound examinations were not standardized, this method represented the actual clinical scenario presented to clinicians in our region. Those patients with >50% internal carotid artery stenosis (including possible occlusion) then underwent CTA and DSA. All CTA and DSA exams were performed within 1 month of each other. Ethical approval for this study was granted from the institution, and informed consent was obtained from each patient.

CT angiography was performed with a GE CTi helical scanner (General Electric, Milwaukee, Wisconsin). A 20 gauge intravenous catheter was placed in an antecubital vein and 120cc. of non-ionic contrast (Omnipaque 300, Nycomed) was infused at 3cc/sec after an initial injection delay. Three mm. helical cuts were made starting from the C6 vertebral body to the skull base. The pitch was 1.5, with 120kV and 200-320 mA. The injection delay time was calculated using the automated program Smartprep® (General Electric) with contrast injection starting was a Hounsfield unit of 40 was detected by a cursor in the common carotid artery at the C6 level. The 3mm axial source images were then reconstructed to 1mm axial cuts. The reconstructed images were then sent to a computer workstation (GE) where generation of 3-D maximum intensity projection (MIP) and shaded surface display (SSD) images was performed. A single investigator (GBA) created all MIP and SSD images. Generation of MIP images was performed using manual editing to exclude all structures except the common, internal, and external carotid arteries in each axial slice. Mural calcification was removed by manual editing on each axial slice. SSD images were produced using a threshold level of 100-300 HU, depending on the degree of luminal contrast. Hard copy images were made rotating the MIP and SSD images every 30 degrees for a total of 360 degrees. The total time to produce the 1mm reconstructed source axial, MIP, and SSD images was 20-25 min per artery.

DSA exams were performed using the transfemoral Seldinger technique. Common and internal carotid arteries were selectively catheterized and lateral, anteroposterior, and lateral oblique images were produced.

The ultrasound, CTA (axial, MIP, SSD), and DSA images were reviewed by three separate investigators blinded to the results of the other two modalities. The degree of stenosis was categorized as follows: 0-29%, 30-49%, 50-69%, 70-99%, and 100%. The CTA and DSA images were measured using calipers and a finely calibrated ruler and the point of maximal stenosis was compared to the normal distal internal carotid diameter (beyond the bifurcation) for degree of stenosis calculation.

Statistical analysis was performed using Spearman correlation coefficient to assess overall agreement. Sensitivity, specificity, positive and negative predictive values, likelihood ratios, and accuracy were used to compare each test to DSA. Statistical significance was calculated using Fisher's exact test.

Results

A total of 40 patients (80 arteries) were studied. Seven source axial, 4 MIP, and 9 SSD images were not included in the data (up to 11% of CTA images were uninterpretable) as they were of poor quality due to motion artifact or poor contrast. Figures 5-1, 5-2 display the raw data comparing the three CTA image types and US with DSA for each degree of stenosis. The agreement was best between axial images and DSA (84%) (fig. 5-1), and worst for US and DSA (49%) (fig. 5-2). All of the image types, especially US, tended to overestimate the degree of stenosis as depicted by DSA.

The overall correlation between CTA, ultrasound (US) and DSA was excellent. CTA correlated with DSA more than US, and the CTA axial images correlated the best overall (table 5-1).

The data was also analyzed for several ranges of stenosis. For occlusion CTA axial images were most accurate (table 5-2). The MIP and SSD images were not as accurate as the axial images for occlusion (fig. 5-3), but were comparable to US. Sensitivity was 100%, specificity 98%, and accuracy 99% for CTA axial images in diagnosing occlusion.

Table 5-3 displays the results of CTA and US in detecting 50-99% stenosis. The axial source images were again the superior modality for this degree of stenosis. The

sensitivity and specificity were 89% and 91%, respectively, with an accuracy of 90%. CTA MIP and SSD images were slightly less accurate than the axial images, but marginally better than US alone. For this degree of stenosis US was highly sensitive (95%) but was not very specific (60%).

For detecting the degree of stenosis of 70-99% the results of CTA and US are presented in table 5-4. Again, CTA axial images were the most accurate for this category. The sensitivity was only 73%, but the axial images were highly specific and accurate, 92% and 89% respectively. MIP and SSD images (figs. 5-4, 5-5) were overall more accurate than US alone, but were inferior to the axial images. US was poorer than all of the CTA image types with a sensitivity, specificity, and accuracy of 82%, 71%, and 73 %, respectively.

CTA and US were also compared to DSA in their ability to detect moderate (50-69%) carotid stenosis (table 5-5). For this degree of stenosis there was little difference between the three CTA image types. Although the CTA images were quite specific (88-93%) and accurate (84-86%), their sensitivities were poor (60-65%). All CTA images were more accurate than US alone. The US images had a very poor sensitivity of 35% for detecting this degree of stenosis.

Since clinicians are usually most concerned with one symptomatic carotid artery, we analyzed the data from just this side alone. We found there was not a significant change in the results when examining just the symptomatic arteries.

US and CTA were also compared for the detection of mild stenosis (0-29%) (table 5-6). For this degree of stenosis CTA was better than US. Of the CTA image types the SSD images were the best with a sensitivity, specificity, and accuracy of 93%, 98%, and 96% respectively. The CTA axial images were also excellent. US was insensitive (57%), but specific (93%) for this degree of stenosis.

The incidence of tandem lesions (17%) was also evaluated. No aneurysms or AVM's were uncovered on the DSA exams, however 2 major intracranial occlusions were noted. There were 11 carotid siphon stenoses discovered by DSA, all of which were mild in degree (<30% luminal reduction). Thirty percent of the bifurcations had moderate to severe calcification of the artery in which it was not possible to assess the degree of stenosis on MIP or SSD images without manually removing the calcification. This heavy

calcification resulted in increased processing time (additional 10 min. per artery) and difficulty distinguishing the true residual lumen. The presence of ulcers was also assessed. There were a total of 9 ulcers detected on the DSA images, and CTA clearly depicted 7 of these (fig. 5-6).

There were no significant complications as a result of the CTA exams. Following the DSA exams there were no reported incidences of major complications (stroke, arterial dissection), and there were few incidences of mild groin hematomas.

Discussion

Doppler ultrasound has been compared to DSA for the detection of carotid stenosis in a number of studies (19, 27-30, 32-35, 43). One study reported a sensitivity and specificity of 96% and 95%, respectively, for stenosis >50% (28). They also reported a sensitivity and specificity of 50% and 95%, respectively, for occlusion. That study, however, did not use color flow doppler (CFD) as is now currently used. CFD has been shown to be more accurate than conventional doppler and also depicts plaque morphology to a greater degree (34). Steinke et al (34) demonstrated accuracies for color flow doppler in the 91-96% range, with the lowest accuracy for more minor stenosis (40-60%). A more recent study (35) of 38 arteries reported perfect sensitivity for >50% and 70-99% stenosis, but poor specificity, 17% and 64%, respectively. They also showed poor sensitivity (63%) and good specificity (90%) for 50-69% stenosis. Our data is in agreement with these results.

Srinivasan et al (33), in a similar study with unstandardized US, reported similar results to ours. They found a sensitivity and specificity for >50% stenosis of 90% and 76%, respectively. They also found US to be more sensitive and specific (92%, 99%) for occlusion than for severe stenosis (71%, 91%), and to be worse for moderate stenosis (69%, 80%).

There have been several studies comparing US to DSA for just severe 70-99% stenosis (27, 29, 30, 32, 43). They report sensitivities and specificities ranging from 81-94% and 83-98%. Their accuracies ranged from 86-95%. Faught et al (29) also reported a sensitivity, specificity, and accuracy of 92%, 97%, and 97%, respectively for 50-69% stenosis. Our own results are poorer than these, possible because our exams were unstandardized. Previous reports have documented the interobserver and intermachine

variability that can occur (19, 31). US results may be more comparable to DSA in those labs that have verified the accuracy of their machine and parameters with DSA.

In the late 1980's it was reported that the carotid artery bifurcation could be visualized with contrast infused CT scanning (44). Since then, using true spiral CT technology, several studies have reported good overall agreement between CTA with DSA for the detection of carotid artery disease (6, 7, 11-13, 16, 21). Schwartz et al (18) provided the first large series of 40 arteries. Their data revealed perfect agreement for occlusion, moderate, and severe stenosis. In their series SSD images were used for stenosis calculation. Other more recent studies have demonstrated near perfect sensitivity and accuracy for occlusion and 80-95% sensitivity for severe (70-99%) stenosis, with detection of moderate stenosis by CTA less sensitive (50-90%) (8, 9, 14, 15, 20, 36).

Sameshima et al (17) recently reported the largest series to date (128 arteries) comparing CTA MIP images with DSA. They found an overall correlation of 0.987. They had perfect agreement for complete occlusions, and sensitivity, specificity, and accuracy of 93%, 100%, and 98%, respectively for 70-99% stenosis. They also reported, as we have here, a poorer degree of accuracy for CTA in detecting moderate degrees of stenosis.

Only one other study has compared axial, MIP, and SSD images in their ability to detect carotid stenosis (10). They reported very similar results to ours with axial images having the highest correlation with DSA (r=.935). Their data also demonstrated excellent accuracy for occlusion and severe stenosis with poorer detection of moderate stenosis.

Our data presented here supports axial images as the most accurate CTA image. Although the 3-D CTA images are more visually appealing to the surgeon (3-D view of location and length of stenosis, location and orientation of calcification) they are less reliable for accurate stenosis calculation. It is also evident, in our data, that CTA is more accurate than unstandardized US in all degrees of stenosis.

In our series, if we used 70-99% stenosis as a definite criterion for surgery, then using CTA axial images would result in 3 (8%) patients wrongfully denied surgery, and 5 (13%) patients wrongfully having surgery (fig. 5-1). Ultrasound was much poorer with 3 (9%) patients wrongfully denied surgery and 15 (47%) patients unnecessarily undergoing surgery (fig. 5-2).

When we separately analyzed the data for just those symptomatic arteries the results changed little. In most cases the accuracy decreased marginally compared to all arteries together.

CTA was excellent at detecting occlusion and >50% stenosis, but with respect to the latter determination it is questionable if this result is precise enough to make a decision with respect to the advisability of surgery. The studies to date have delineated specific ranges of stenosis that benefit differently from surgery. It is desirable that imaging accurately distinguish between them. In this study CTA was unable to detect with a high degree of sensitivity those arteries which were 50-69% versus those 70-99% stenosed.

Although CTA has the advantages of being a minimally invasive test, the significant processing time to generate images (20-25 min./artery) and the less than ideal accuracy make it less attractive than initially thought. Even in experienced hands, severe calcification increases the processing time and makes determination of the true residual lumen difficult. DSA has significant risks associated with it, however there is important additional information it provides that CTA cannot: intracranial pathology, collateral flow patterns, precise stenosis determination, and the presence of intracranial tandem stenosis. Recently Kappelle et al (45) reported that the presence of carotid siphon stenosis influences the risk/benefit ratio for those patients with 50-69% stenosis. Since CTA cannot provide this information a decision on the most appropriate management protocol, based solely on CTA, can be incorrect.

In conclusion, without standardization we found US to be relatively inaccurate in the quantification of carotid stenosis. CTA was found to be superior to US, and the source axial CTA images to be more accurate than the 3-D reconstructed images. Weighing the advantage of being less invasive with the disadvantages of being less accurate and not providing as much information as DSA, CTA does not appear, at this point, to be an optimal replacement for DSA in the investigation of carotid disease. Early studies to date indicate MRA may be a more attractive alternative to DSA than CTA (14).

DSA	CTA 0-29%	CTA 30-49%	CTA 50-69%	CTA 70-99%	CTA 100%
100%		1		*4*, 3	**13**, *9*, 9
70-99%		1	**2**, *2*, 2	**8**, *10*, 8	**1**, *1*, 1
50-69%	**2**, *2*, 1	1	**10**, *11*, 9	**4**, *5*, *4*	
30-49%		**4**, 1	*3*, 1	**1**, 1	
0-29%	**26**, *23*, 27	**1**, *5*, 1	**1**, 1	*1*	

Fig. 5-1 CTA **axial**, *MIP*, SSD images compared to DSA by degree of stenosis, number of arteries

	100%				3	7
	70-99%			1	8	2
DSA	50-69%	2		6	9	
	30-49%	1			1	
	0-29%	10	4	7	2	
		0-29%	30-49%	50-69%	70-99%	100%
				US		

Fig. 5-2 Ultrasound compared to DSA, number of arteries, total n=63

Figure 5-3

Occlusion of internal carotid artery (arrow) on CTA SSD (a), MIP (b), and DSA (c).

Figure 5-4

Carotid stenosis (arrow) seen on DSA (a), MIP (b), and SSD (c) images.

Figure 5-5

Severe carotid stenosis (arrow) shown on DSA (a), MIP (b), and SSD (c) images.

Figure 5-6

Severe carotid stenosis with ulcer (arrow) shown on DSA (a), MIP (b), and SSD (c) images.

Table 5-1 Correlation between CTA, US with DSA

		r*
CTA	axial	0.922
	MIP	0.892
	SSD	0.917
US		0.808

r= Spearman correlation coefficient, P=0.01

Table 5-2 Statistics Comparing CTA & US with DSA for 100% Stenosis

Modality	Sens.	Spec.	PPV	NPV	"+" LR	"-" LR	Acc.	P value
axial	1	0.98	0.93	1	50	0	0.99	<.001
MIP	0.69	0.98	0.9	0.94	34.5	0.32	0.93	<.001
SSD	0.75	0.98	0.9	0.95	37.5	0.26	0.94	<.001
US	0.7	0.96	0.78	0.94	17.5	0.3	0.92	<.001

Sens.= sensitivity, spec.= specificity, PPV= positive predictive value, NPV= negative predictive value, +LR= positive likelihood ratio, -LR= negative likelihood ratio,. Acc.= accuracy

Table 5-3 Statistics Comparing CTA & US with DSA for >50% Stenosis

Modality	Sens.	Spec.	PPV	NPV	"+" LR	"-" LR	Acc.	P value
axial	0.89	0.91	0.86	0.93	9.9	0.12	0.9	<.001
MIP	0.9	0.82	0.78	0.93	5	0.12	0.86	<.001
SSD	0.85	0.86	0.75	0.9	6.1	0.17	0.86	<.001
US	0.95	0.6	0.78	0.88	2.4	0.08	0.81	<.001

Sens.= sensitivity, spec.= specificity, PPV= positive predictive value, NPV= negative predictive value, +LR= positive likelihood ratio, -LR= negative likelihood ratio, Acc.= accuracy

Table 5-4 Statistics Comparing CTA & US with DSA for 70-99% Stenosis

Modality	Sens.	Spec.	PPV	NPV	"+" LR	"-" LR	Acc.	P value
axial	0.73	0.92	0.62	0.95	9.1	0.29	0.89	<.001
MIP	0.77	0.84	0.5	0.95	4.8	0.27	0.83	<.001
SSD	0.67	0.86	0.5	0.93	4.8	0.38	0.83	<.001
US	0.82	0.71	0.38	0.95	2.8	0.25	0.73	0.002

Sens.= sensitivity, spec.= specificity, PPV= positive predictive value, NPV= negative predictive value, +LR= positive likelihood ratio, -LR= negative likelihood ratio, Acc.= accuracy

Table 5-5 Statistics Comparing CTA & US with DSA for 50-69% Stenosis

Modality	Sens.	Spec.	PPV	NPV	"+" LR	"-" LR	Acc.	P value
axial	0.65	0.91	0.69	0.89	7.2	0.38	0.85	<.001
MIP	0.61	0.88	0.69	0.88	5.1	0.44	0.84	<.001
SSD	0.6	0.93	0.69	0.89	8.6	0.43	0.86	<.001
US	0.35	0.87	0.5	0.78	2.7	0.75	0.73	0.07

Sens.= sensitivity, spec.= specificity, PPV= positive predictive value, NPV= negative predictive value, +LR= positive likelihood ratio, -LR= negative likelihood ratio, Acc.= accuracy

Table 5-6 Statistics Comparing CTA & US with DSA for 0-29% Stenosis

		Sens.	Spec.	PPV	NPV	"+" LR	"-" LR	Acc.
CTA	axial	0.9	0.95	0.93	0.93	18	0.1	0.93
	MIP	0.79	0.96	0.92	0.88	19.8	0.22	0.89
	SSD	0.93	0.98	0.96	0.95	46.5	0.07	0.96
US		0.57	0.93	0.81	0.79	8.1	0.46	0.79

P<0.001

Sens.= sensitivity, spec.= specificity, PPV= positive predictive value, NPV= negative predictive value, +LR= positive likelihood ratio, -LR= negative likelihood ratio, Acc.= accuracy

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Conclusions

Cerebrovascular disease is a major component of present neurosurgical practice. This includes, among other things, diagnosis and treatment of ruptured intracranial aneurysms, identification of cerebral vasospasm post aneurysm rupture, and detection and precise quantification of carotid artery stenosis. Presently the accepted method for diagnosing these three entities is digital subtraction angiography (DSA). This modality, however, is not without patient risk, vascular injury, arterial dissection, and stroke are among several potential complications (2, 5, 10, 11). It is also a costly and time-consuming method for imaging the cerebral vessels. As technology advances new, cheaper, less invasive, and less patient risk modalities are introduced in the hope of replacing the old more risky methods. CT angiography (CTA) is one of these newer modalities. This new modality needs to be shown to have comparable accuracy compared to DSA before it can replace DSA for investigating cerebrovascular disease. The purpose of the work presented here was multiple: to develop a protocol for CTA of the cerebral vessels and carotid bifurcation; to compare CTA with DSA in the detection of cerebral aneurysms following subarachnoid hemorrhage (SAH); to determine if CTA could replace DSA in the diagnosis and management of ruptured cerebral aneurysms; to compare CTA to DSA in the detection and quantification of cerebral vasospasm following SAH; and to compare CTA to DSA in the detection and quantification of carotid artery stenosis.

In the first part of this study we compared CTA to DSA in the detection of cerebral aneurysms following SAH. In a sample of 40 patients we found CTA to have a sensitivity and specificity, for aneurysm presence alone, of 86% and 90%, respectively. These results are similar to previously published results by other institutions (1, 3, 7, 9). CTA was also found to be >95% accurate in determining dome and neck size, aneurysm lobularity, and the presence and number of adjacent arterial branches. CTA correctly determined the direction of filling of anterior communicating artery aneurysms by examining neck location, direction of aneurysm protrusion, and the larger feeding first segment of the anterior cerebral artery. The 3-dimensional representation provided by CTA was considered useful for surgical planning. The difficulty found with CTA in this initial study, was the inability to detect aneurysms <4mm. in size, and those of the juxtasellar internal carotid artery. This difficulty has also been reported by others (3, 7).

In the next section the question "can CTA replace DSA in the diagnosis and operative planning of ruptured cerebral aneurysm" was examined. In a sample of 173 patients it was found that CTA could replace DSA in 48% of patients undergoing surgical treatment. The location of the aneurysm predicted whether the patient also underwent DSA prior to surgery with middle cerebral artery aneurysms less likely, and posterior communicating artery aneurysms more likely to require the additional DSA. In this series of patients, the sensitivity and specificity for aneurysm detection by CTA was 84-90% and 100%, respectively. These results are consistent with those in the previous section as well as those published by others (1, 3, 7, 9). Those false negative CTA aneurysms in this series were, again, <4mm. in size and were usually found in patients with multiple aneurysms where the larger, ruptured aneurysm was identified by CTA. Cavernous internal carotid artery aneurysms were very difficult to detect with CTA, however they do not require treatment.

A not infrequent complication of SAH is cerebral vasospasm which may occur 5-15 days post bleed. Patients sustaining SAH are monitored and investigated for the development of vasospasm as adequate early treatment may prevent serious ischemic brain damage. Currently, DSA is the modality of choice to accurately diagnose vasospasm. In the next section of this study we examined the ability of CTA to accurately detect and quantify vasospasm compared to DSA. A total of 17 patients were studied and the highest correlation (.88-.998) between CTA and DSA was for proximal arterial locations (internal carotid artery, first segments of the anterior and middle cerebral arteries). The agreement between CTA and DSA was also greater for none or severe vasospasm than for mild or moderate spasm. CTA tended to overestimate the degree of vasospasm. The sensitivity and accuracy was greater for proximal locations and in detecting none or severe vasospasm than for distal locations or detecting mild or moderate spasm. We found that 9% of the arteries and all the clip-aneurysm complexes could not be assessed by CTA due to aneurysm clip artifact. There has been little in the literature comparing CTA with DSA for the detection of cerebral vasospasm, but one recent study reported perfect agreement between CTA and DSA for detecting severe vasospasm (8). This is in accordance with our data.

The other major use of DSA in cerebrovascular neurosurgery is in the diagnosis of carotid bifurcation stenosis. The last part of the study compared CTA and ultrasound (US) to DSA in 80 arteries for the detection and quantification of carotid stenosis. It was found that CTA axial images correlated with DSA more than CTA MIP (maximum intensity projection) or CTA SSD (shaded surface display) or US images. This echoes previous reports (4). CTA and US tended to overestimate the degree of stenosis compared to DSA. It was also found that CTA was more sensitive and accurate in all degrees of stenosis than US. CTA was extremely sensitive (89-100%) and accurate (90-99%) in detecting 50-99% and 100% stenosis. The sensitivity and accuracy of CTA for 70-99% and 50-69% stenosis was poorer; 65-73%, 85-89%, respectively. In our series, 30% of arteries had calcification to the extent that the CTA images could not be assessed without time consuming manual removal, this difficulty of CTA has been reported by others as well (5).

The ultimate objective of this study was to determine if CTA could replace DSA in cerbrovascular neurosurgery. From the first two sections in this study we have found CTA to have adequate sensitivity and specificity in detecting cerebral aneurysms in the setting of SAH. Furthermore, CTA can replace DSA in the preoperative planning of these aneurysms in about 50% of cases. We also examined the accuracy of CTA in detecting vasospasm following SAH and found CTA to be highly sensitive and accurate for detecting none or severe spasm in proximal locations, however, we also found that the aneurysm-clip complex and 9% of arteries could not be assessed due to aneurysm clip artifact on CTA. These difficulties negate any benefits CTA has over DSA and thus CTA is unlikely to replace DSA in this capacity. We then compared CTA to DSA in the detection and quantification of carotid stenosis and found that the 2-dimensional CTA axial images to be more accurate than the 3-dimensional CTA images (MIP, SSD). CTA was excellent at detecting >50% and 100% stenosis, but was unable to detect with a high sensitivity 70-99% or 50-69% stenosis. These results and the fact that CTA does not provide the extra information of DSA (tandem stenosis, crossflow, intracranial pathology) make it unlikely at this point for CTA to replace DSA in the investigation of carotid disease.

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